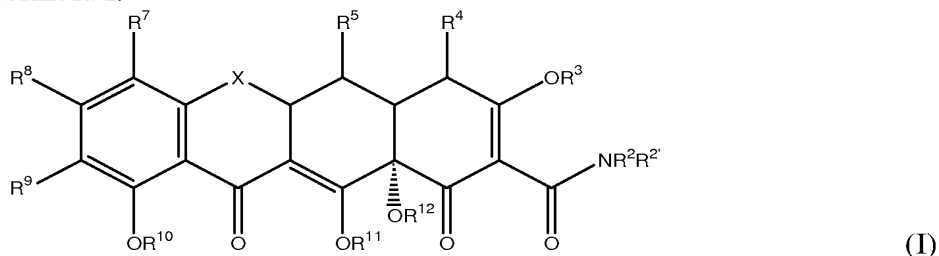


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of the claims and listing of the claims in the application:

1. **(Previously Presented)** A method for treating or preventing malaria in a subject, comprising administering to said subject an effective amount of a substituted tetracycline compound of formula I:



wherein:

X is CR^{6'}R⁶;

R², R^{2'}, R^{4'}, and R^{4''} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ is NR^{4'}R^{4''}, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R³, R¹¹ and R¹² are each hydrogen, or a pro-drug moiety;

R¹⁰ is hydrogen, or a prodrug moiety;

R⁵ is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R⁶ and R^{6'} are independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R⁷ is aryl;

R⁹ is hydrogen;

R⁸ is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and pharmaceutically acceptable salts thereof, such that malaria is treated or prevented in said subject.

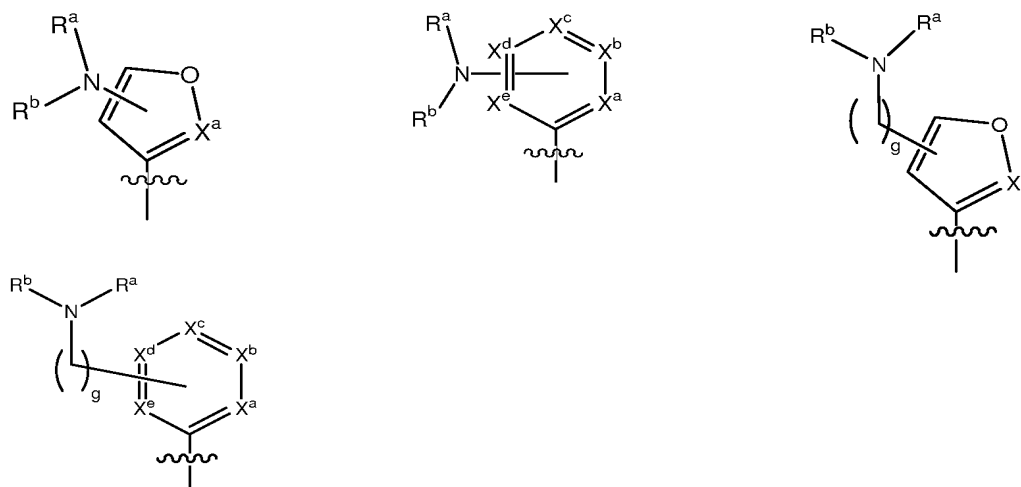
2. **(Cancelled)**

3. **(Previously Presented)** The method of claim 1, wherein R², R^{2'}, R³, R⁸, R¹⁰, R¹¹, and R¹² are hydrogen; R⁴ is NR^{4'}R^{4''}; R^{4'} and R^{4''} are alkyl, and X is CR⁶R^{6'}.

4. **(Previously Presented)** The method of claim 3, wherein R⁵, R⁶, and R^{6'} are each hydrogen.
5. **(Previously Presented)** The method of claim 3, wherein R⁵ is hydroxy or a prodrug moiety, R⁶ is methyl and R^{6'} is hydrogen.
- 6 - 28. **(Cancelled)**
29. **(Previously Presented)** The method of claim 1, wherein R⁷ is substituted or unsubstituted phenyl.
30. **(Previously Presented)** The method of claim 29, wherein R⁷ is substituted with halogen, alkoxy, amino, acyl, alkyl, nitro, formyl, amido, alkyl, alkenyl, alkynyl, or aryl.
31. **(Previously Presented)** The method of claim 30, wherein R⁷ is substituted with is methoxy, ethoxy, propoxy, methylene dioxy, or ethylene dioxy.
32. **(Previously Presented)** The method of claim 30, wherein R⁷ is substituted with substituted or substituted methyl, ethyl, propyl, butyl or pentyl.
33. **(Previously Presented)** The method of claim 32, wherein said substituted or substituted methyl, ethyl, propyl, butyl or pentyl is substituted with an amino, carbocyclic or heterocyclic group.
34. **(Previously Presented)** The method of claim 30, wherein R⁷ is substituted with acetyl.
35. **(Previously Presented)** The method of claim 28, wherein R⁷ is substituted or unsubstituted heteroaryl.
36. **(Previously Presented)** The method of claim 35, wherein R⁷ is thienyl, imidazolyl, pyrrolyl, pyridinyl, furanyl, pyrimidinyl, or benzofuranyl.
- 37 - 41. **(Canceled)**

42. **(Previously Presented)** The method of claim 1, wherein R⁷ comprises an ionizable nitrogen atom.

43. **(Currently Amended)** The method of claim ~~26~~ 1, wherein R⁷ is selected from the group consisting of:



wherein:

R^a and R^b are each independently hydrogen, halogen, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, or heterocyclic;

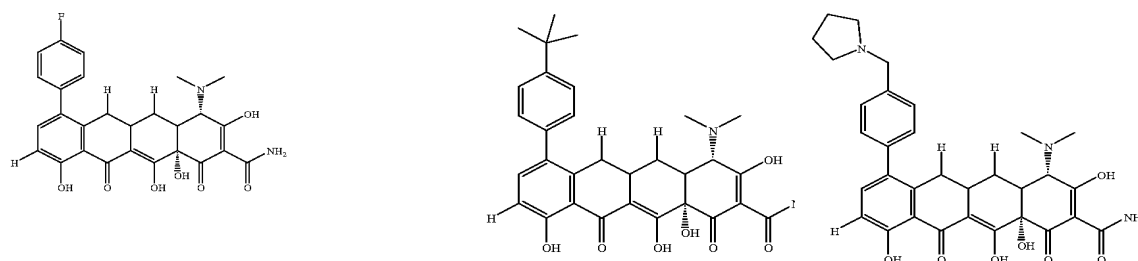
g is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20;

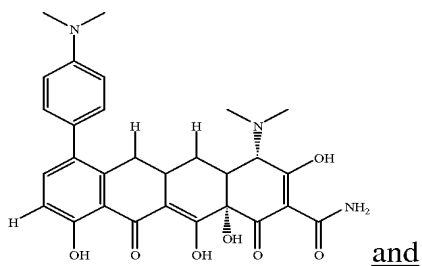
n is 0, 1, 2, or 3; and

X^a, X^b, X^c, X^d, and X^e are each independently optionally substituted carbon, oxygen, nitrogen, or sulfur.

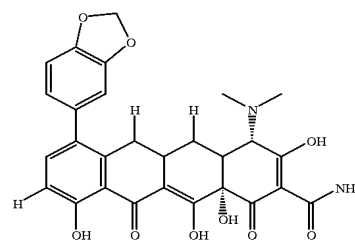
44 – 47. **(Cancelled)**

48. **(Currently Amended)** The method of claim 1, wherein said compound is selected from the group consisting of:

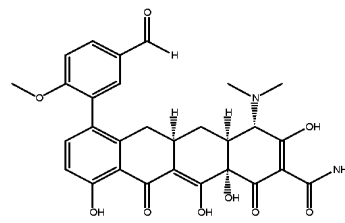
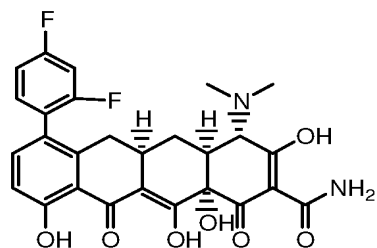
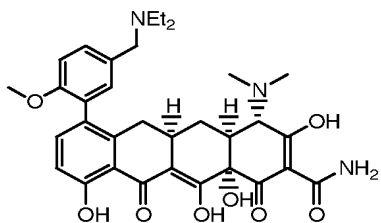
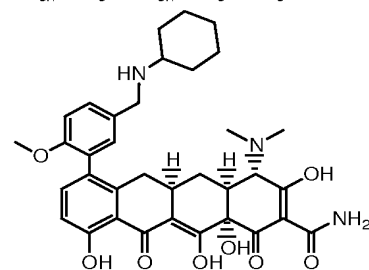
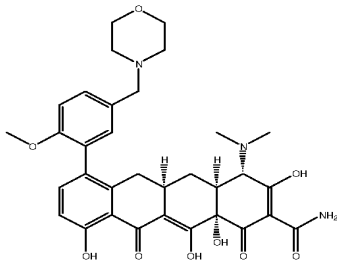
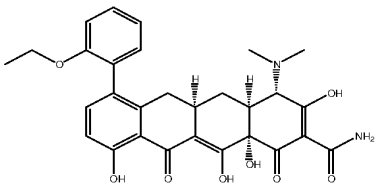
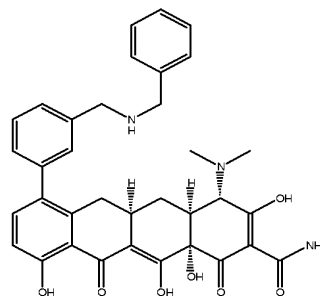
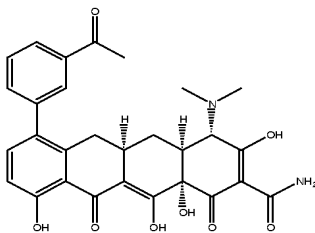
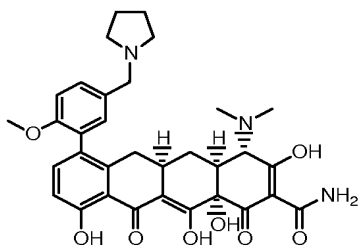
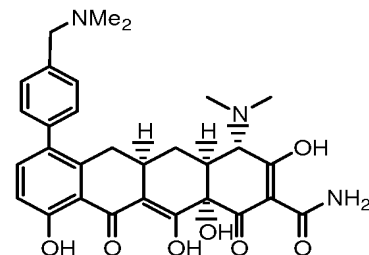
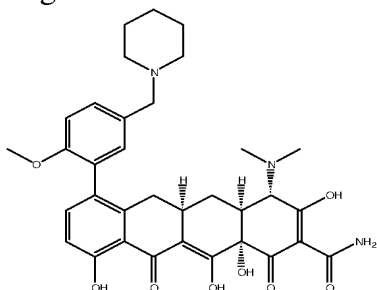
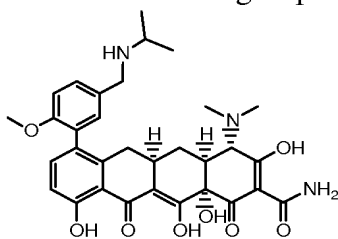


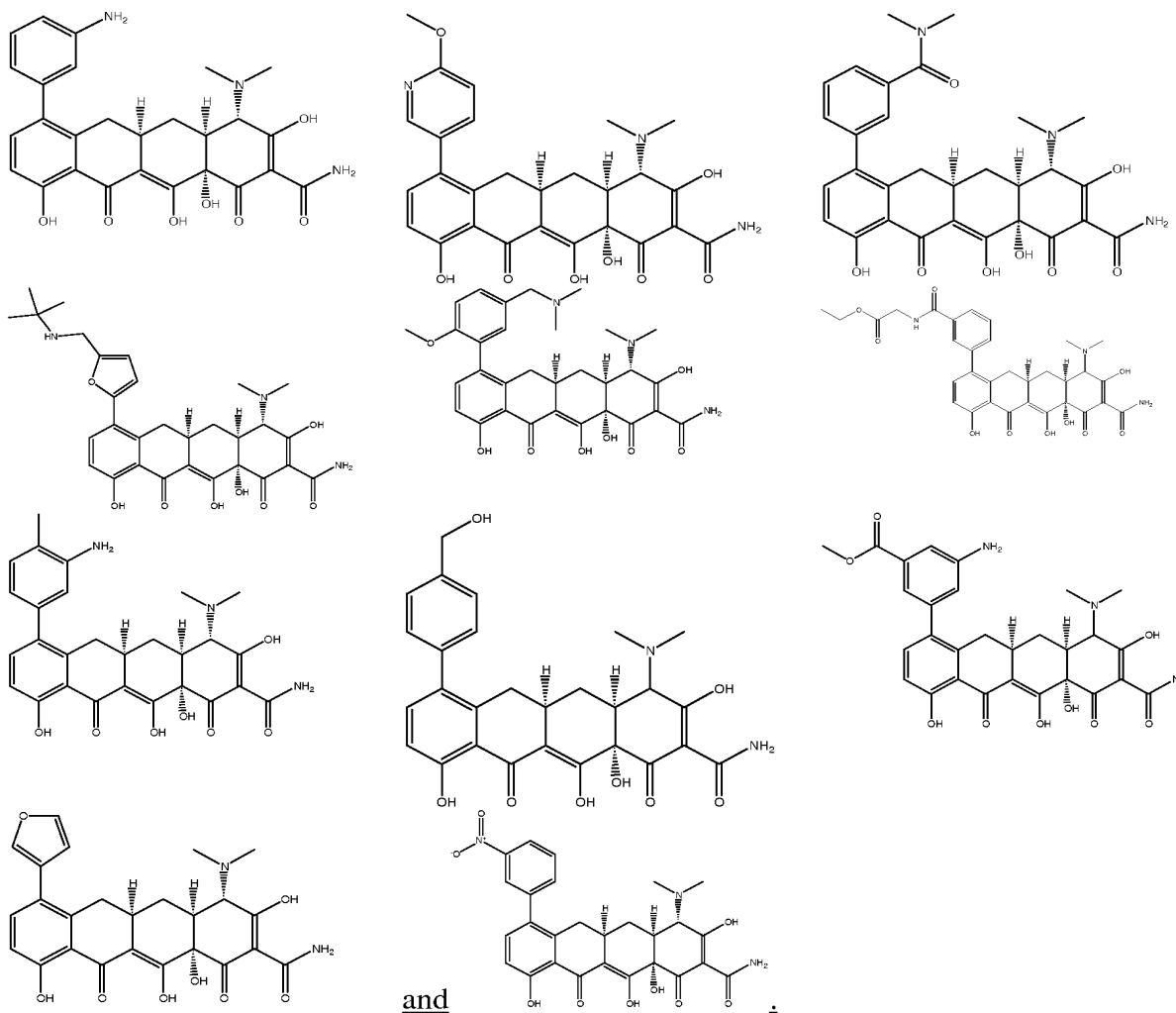


and

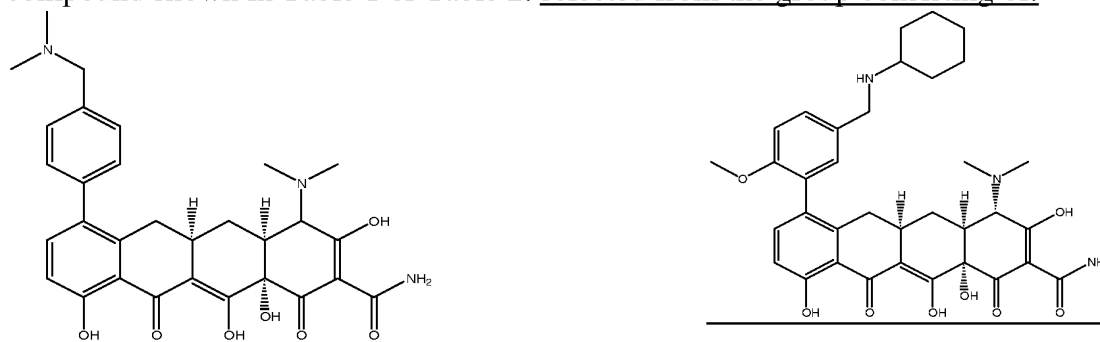


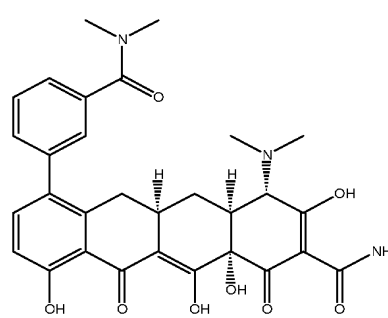
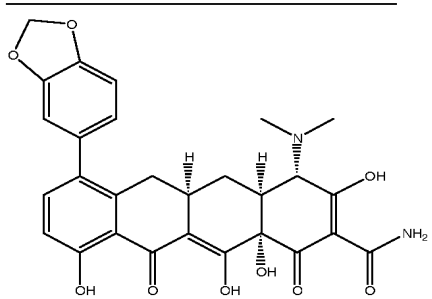
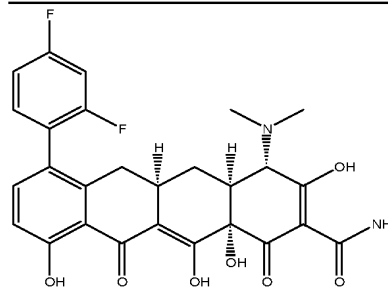
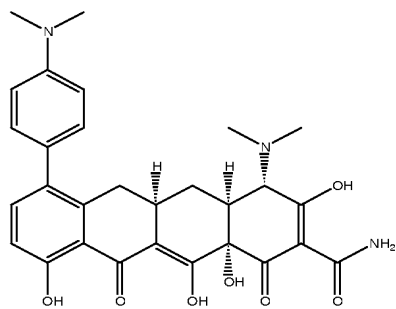
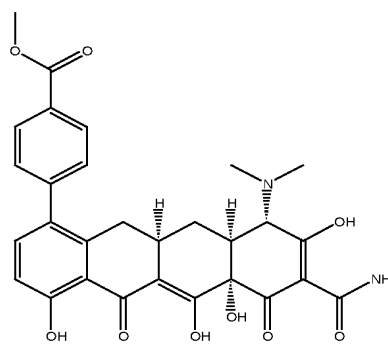
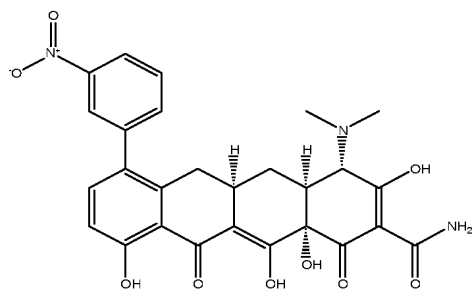
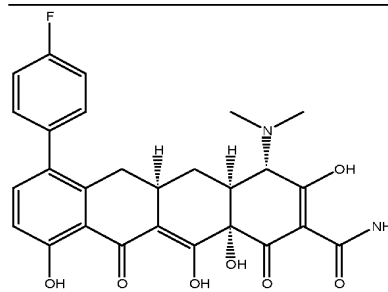
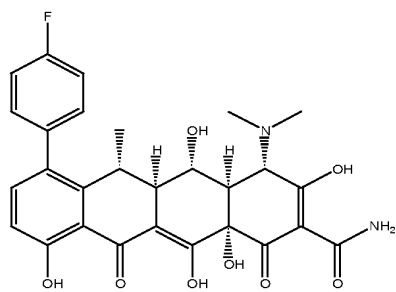
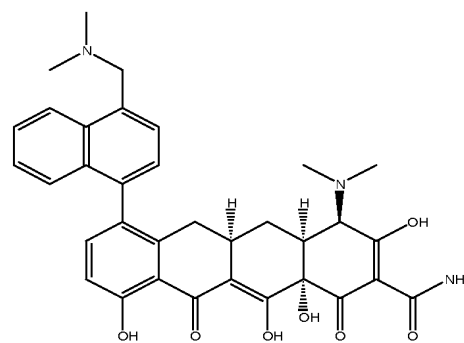
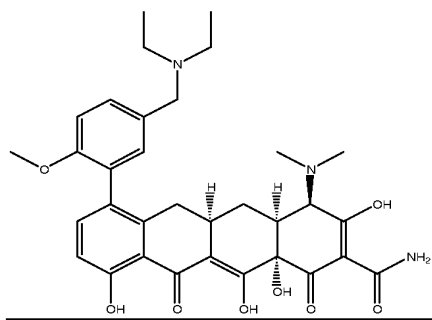
49. **(Currently Amended)** The method of claim 1, wherein said compound is selected from the group consisting of:

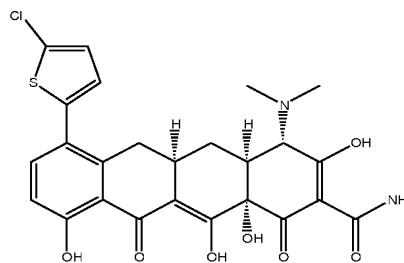
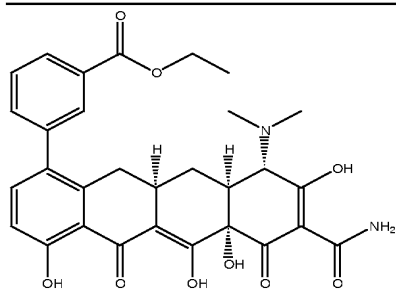
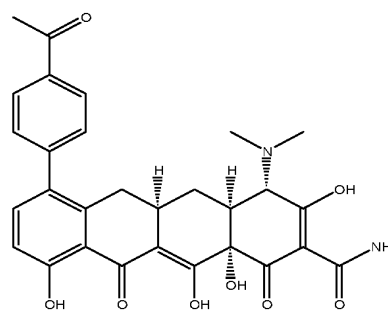
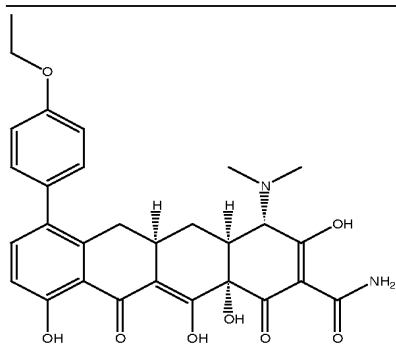
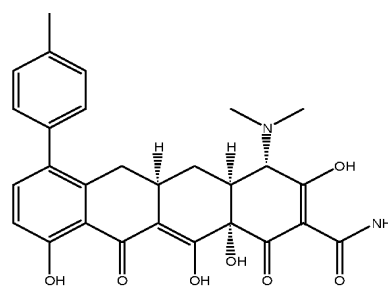
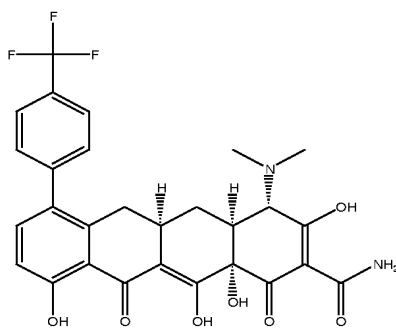
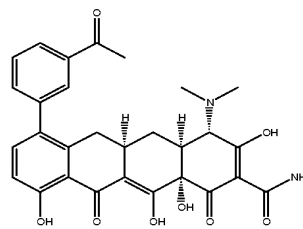
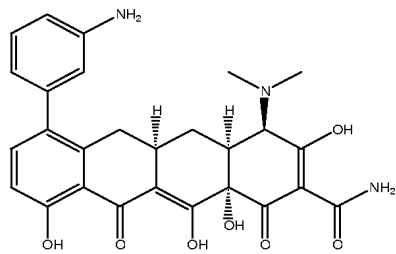
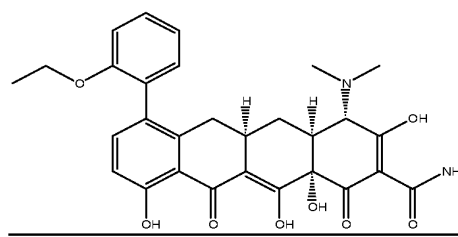
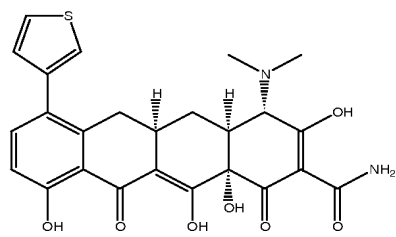


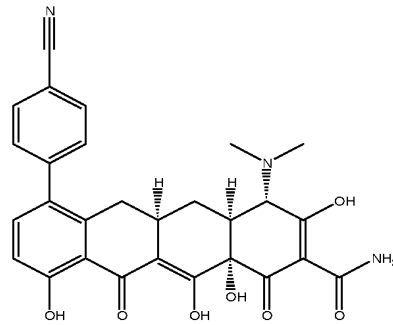
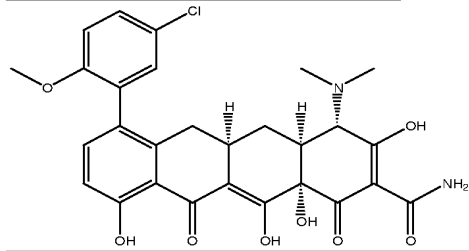
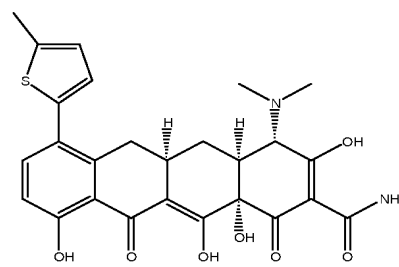
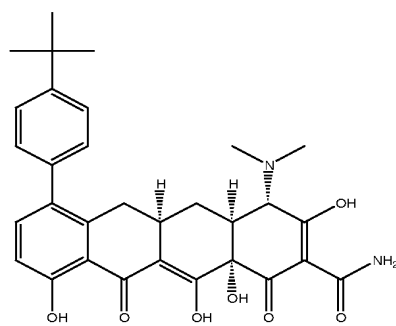
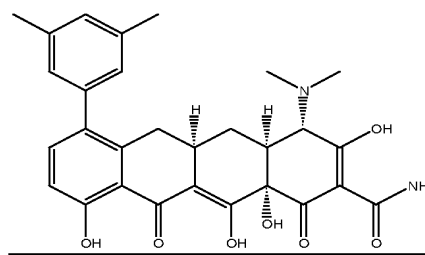
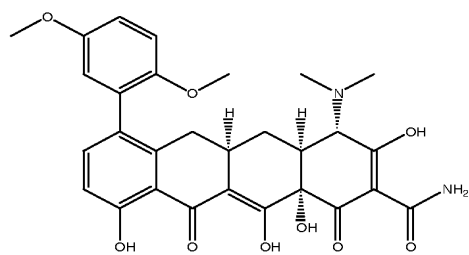
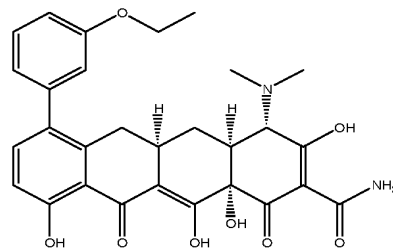
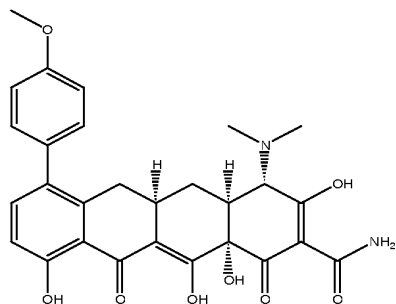
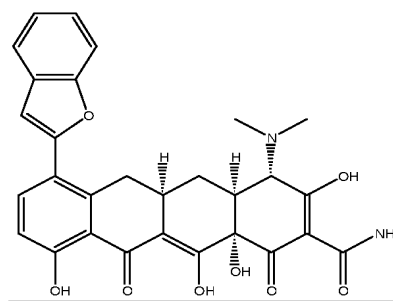
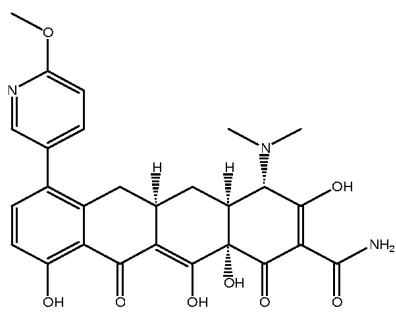


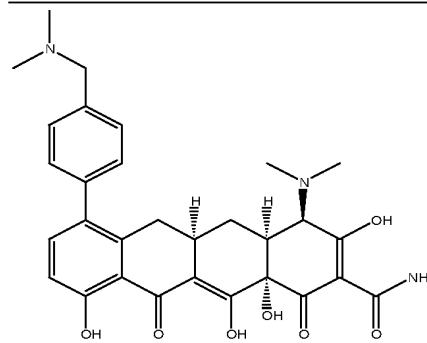
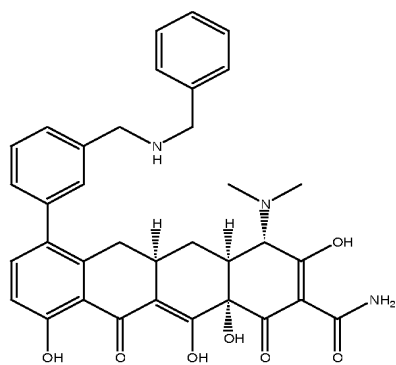
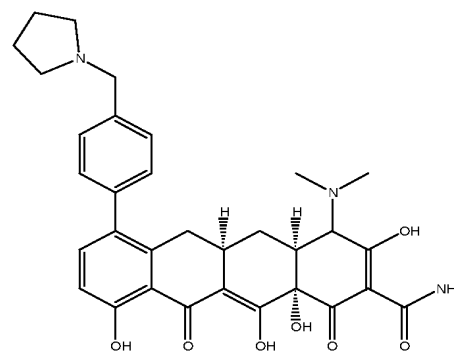
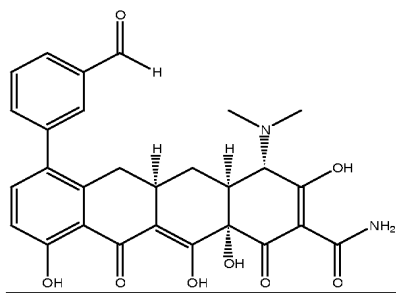
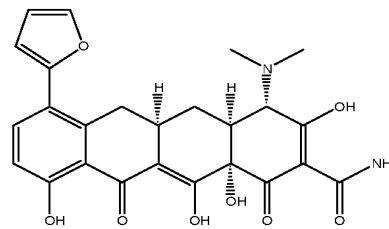
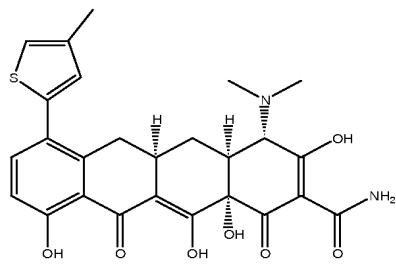
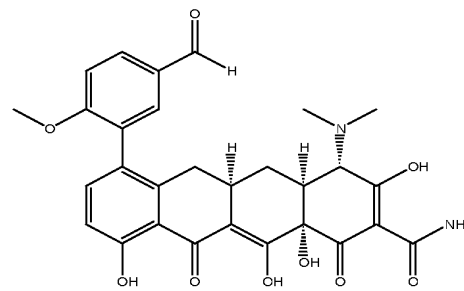
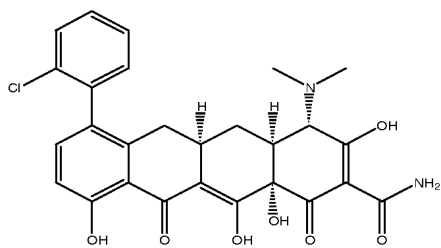
50. (Currently Amended) The method of claim 1, wherein said compound is a compound shown in Table 1 or Table 2, selected from the group consisting of:

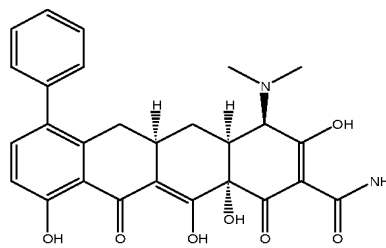
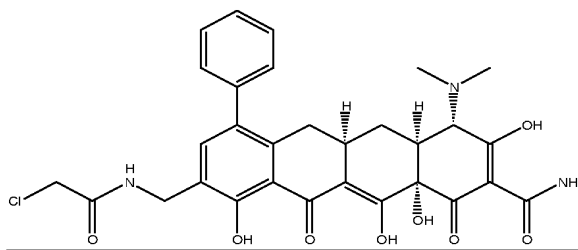
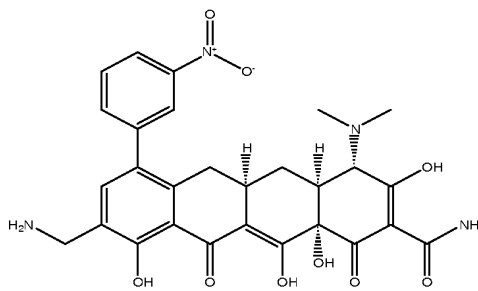
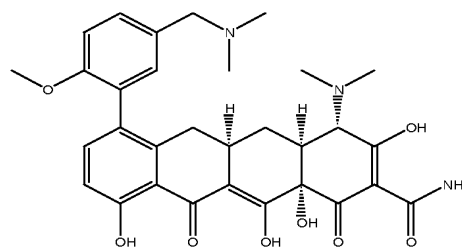
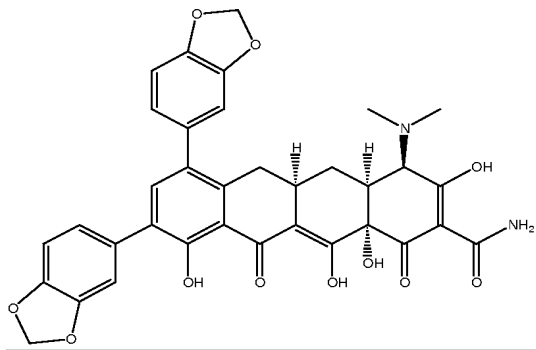
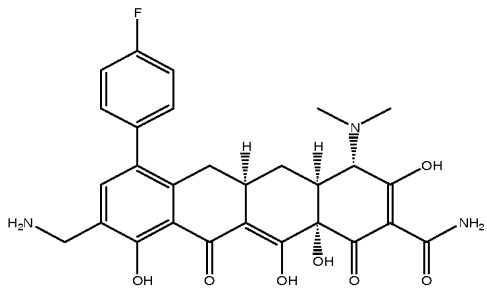
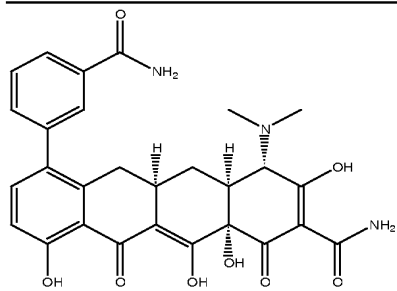
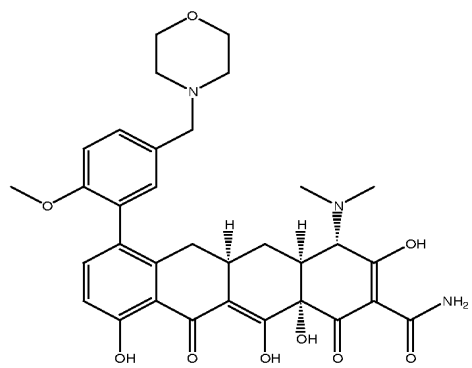


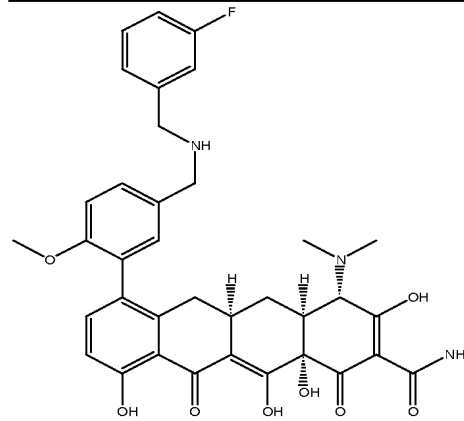
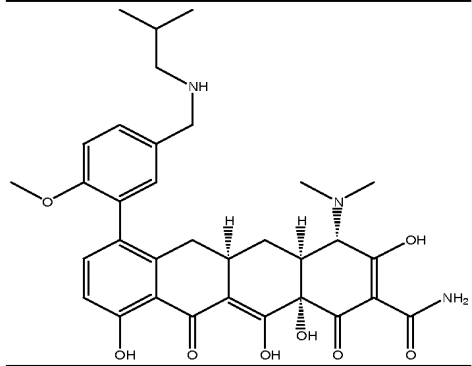
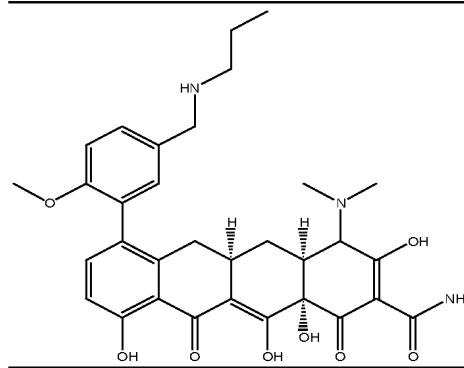
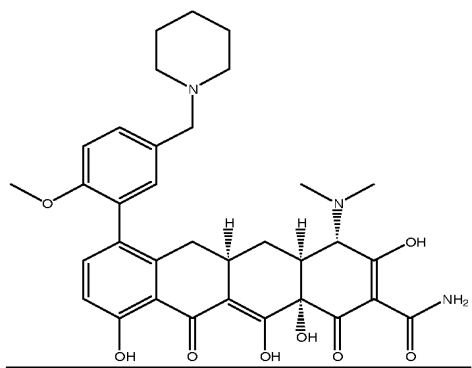
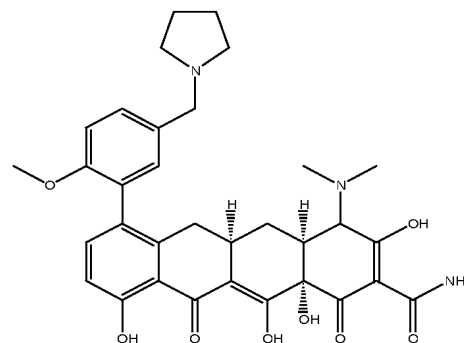
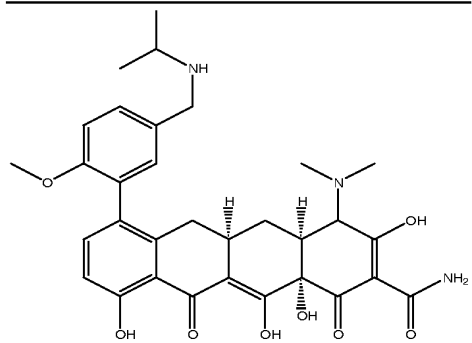
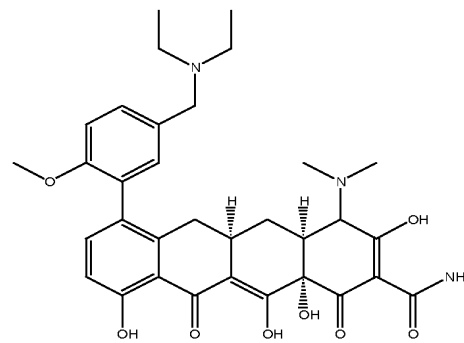
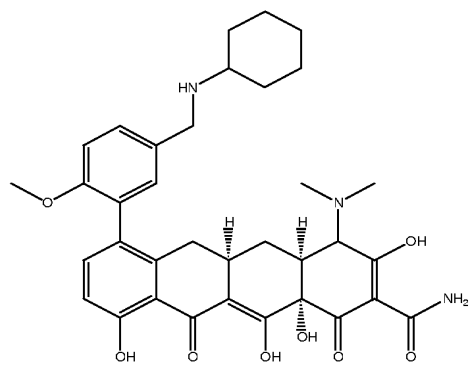


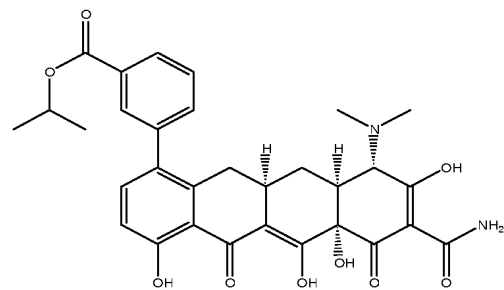
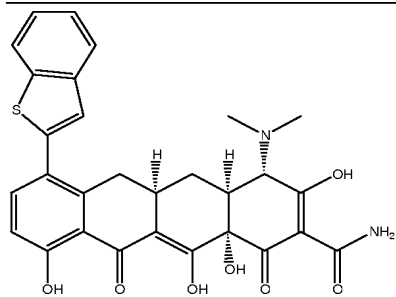
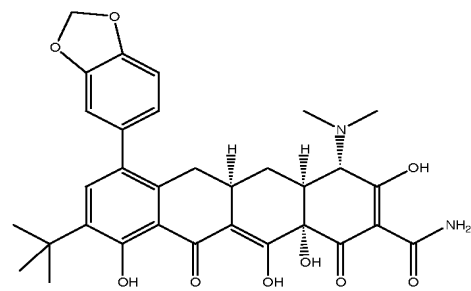
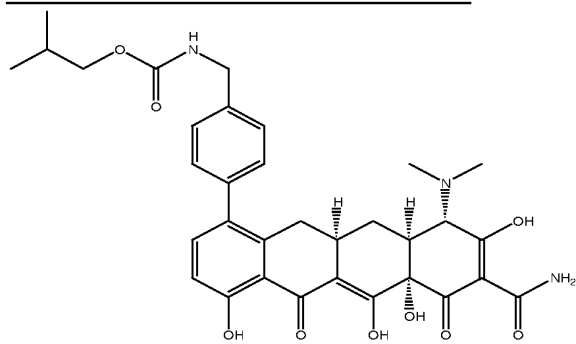
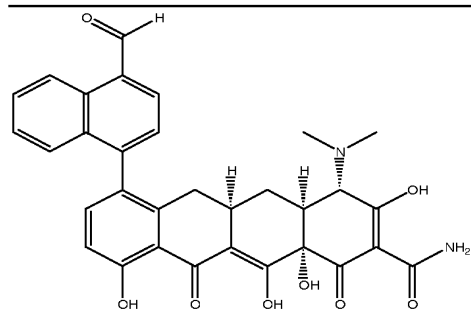
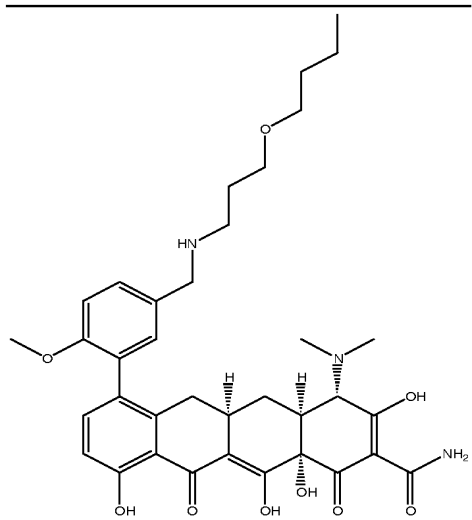
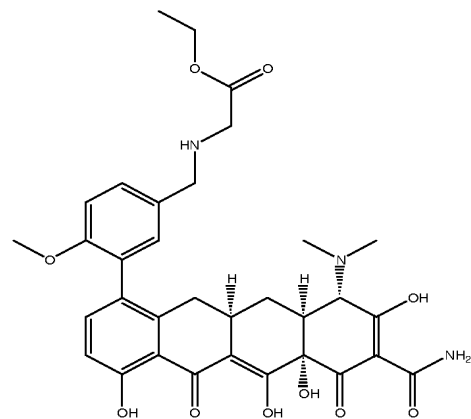
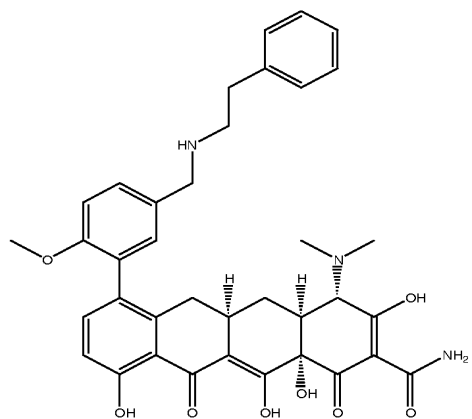


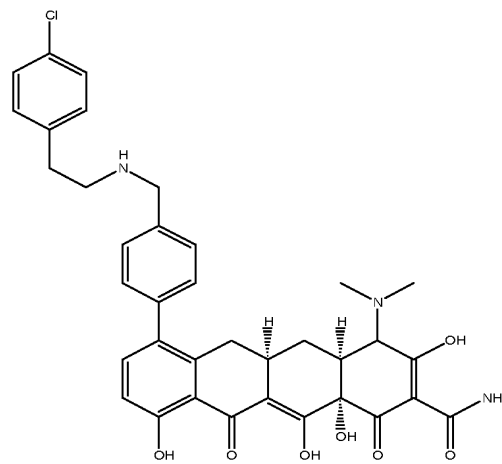
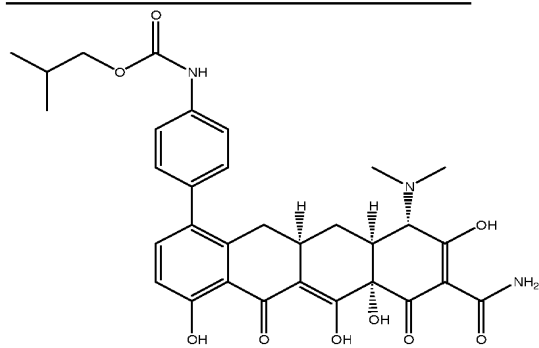
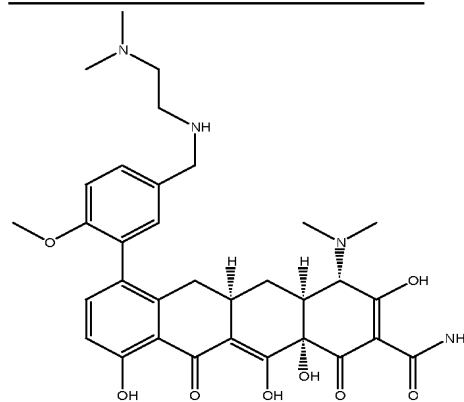
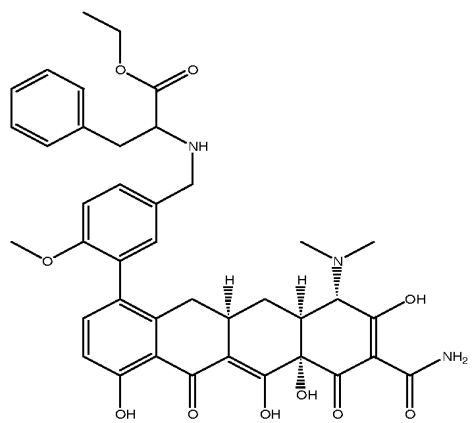
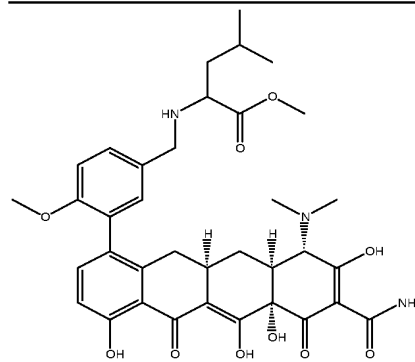
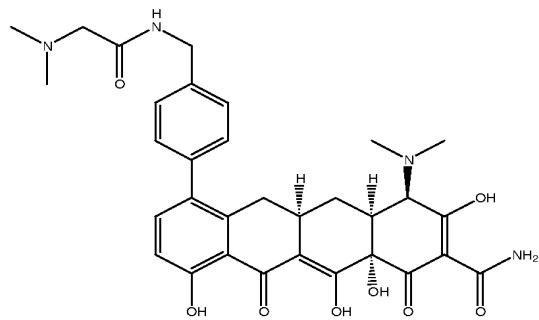
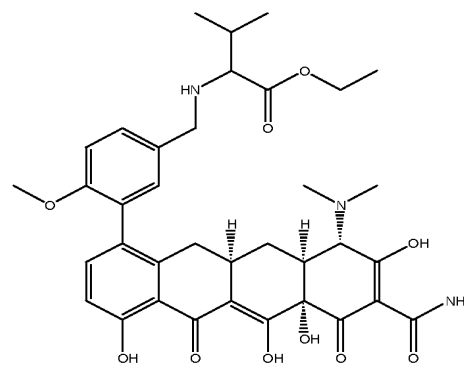
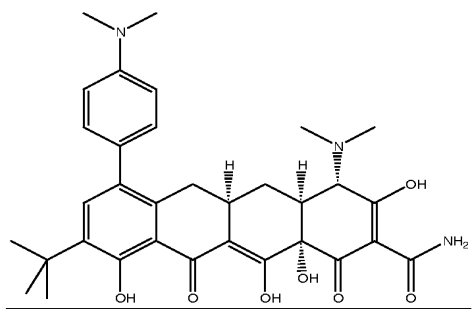


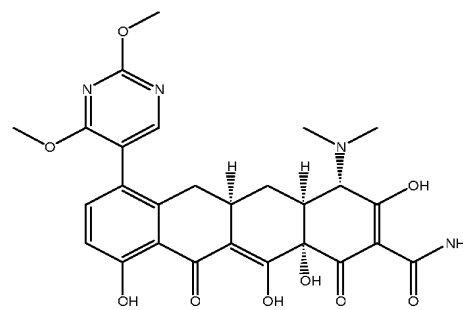
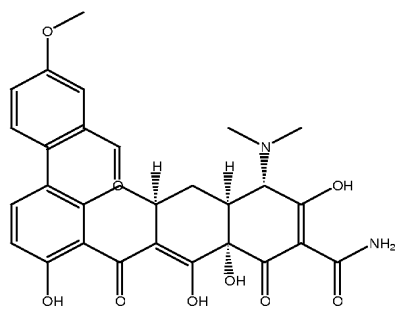
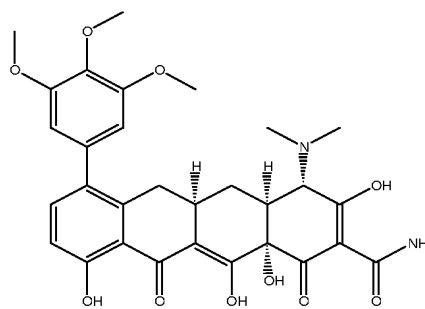
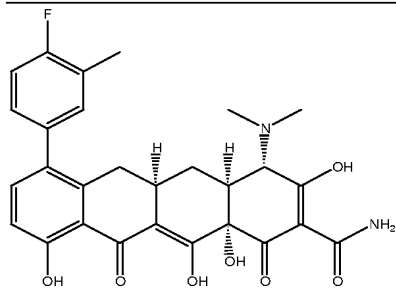
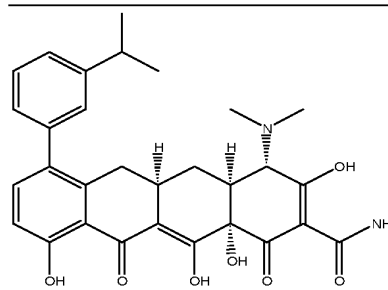
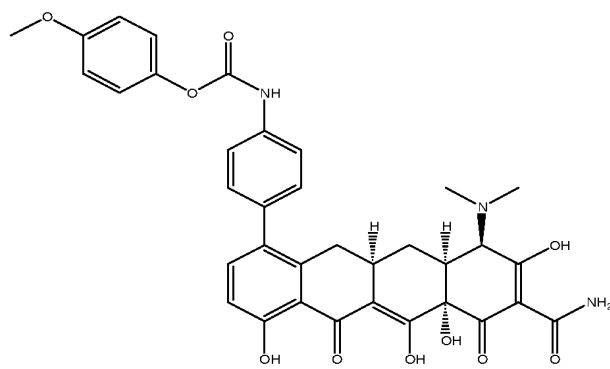
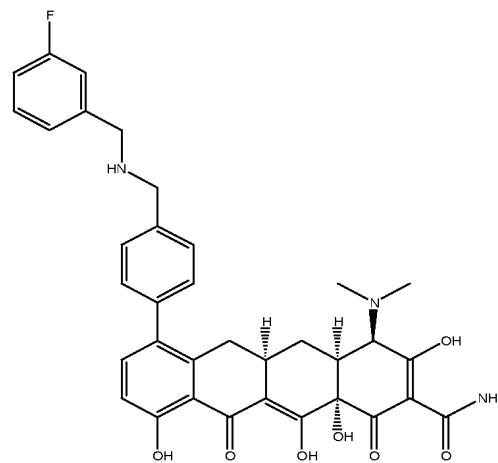
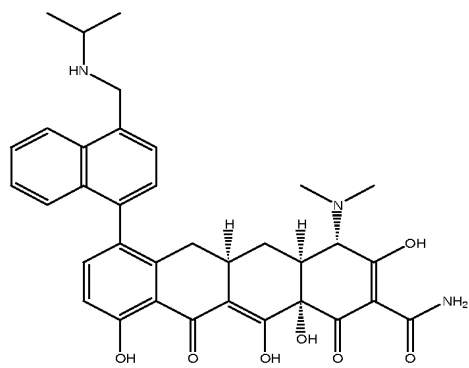


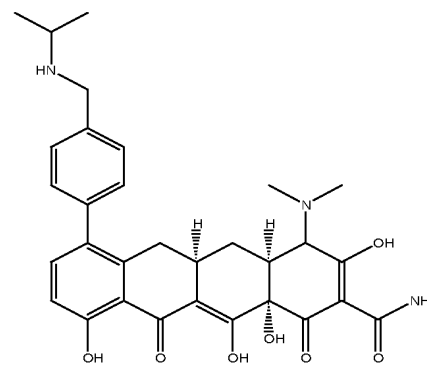
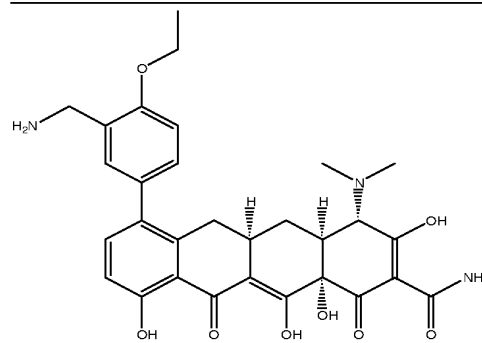
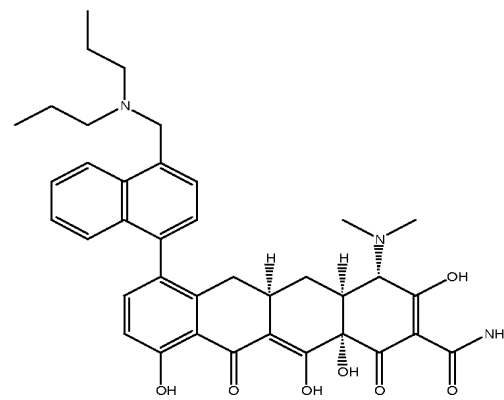
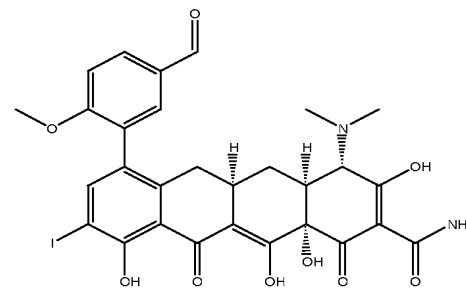
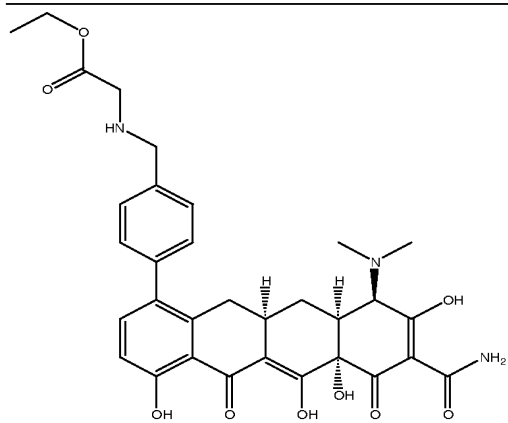
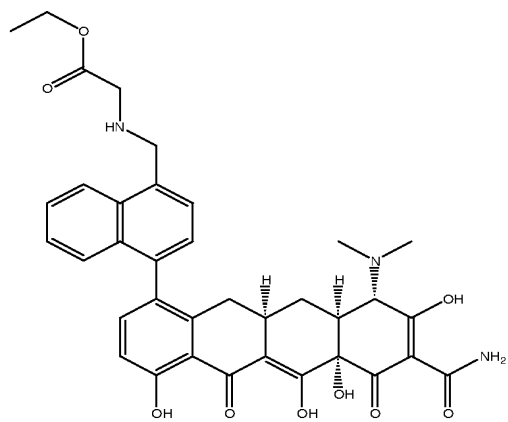
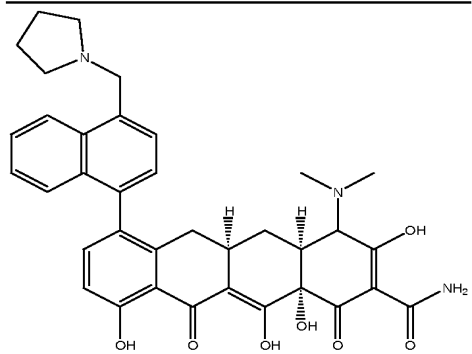
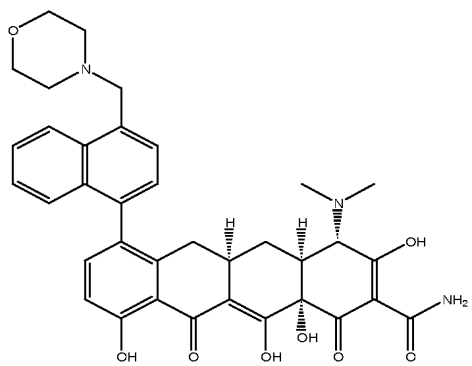


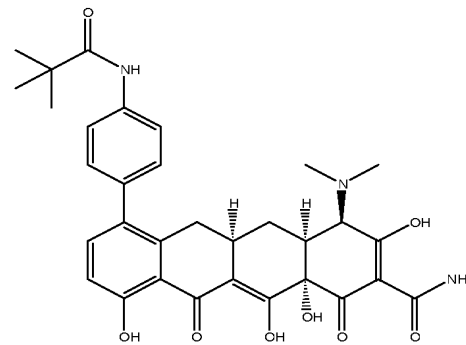
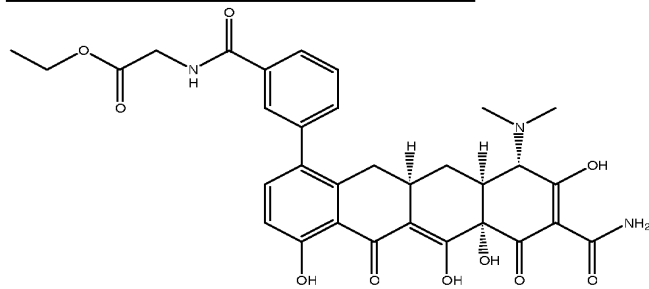
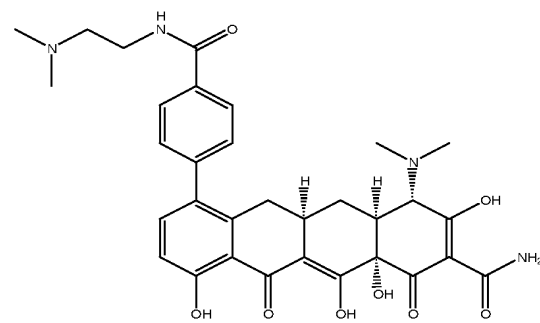
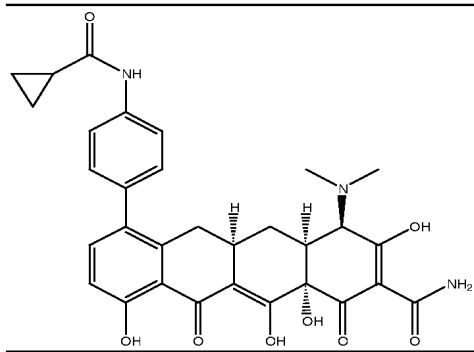
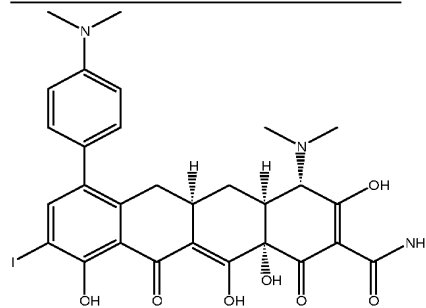
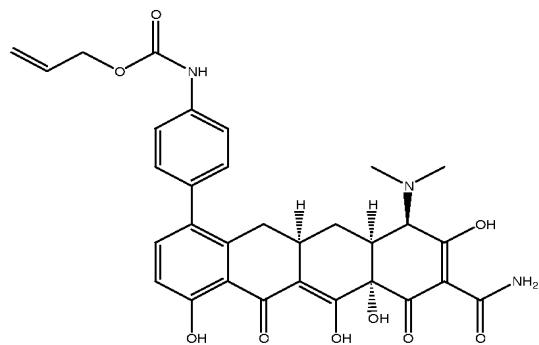
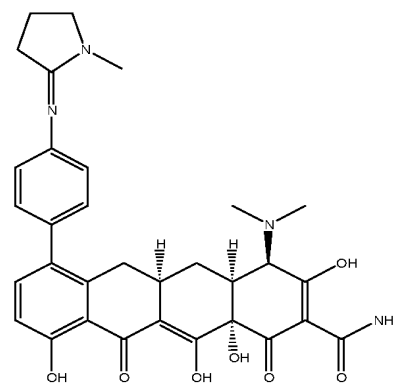
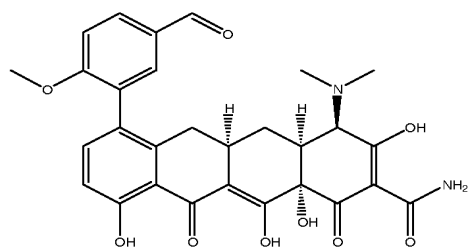


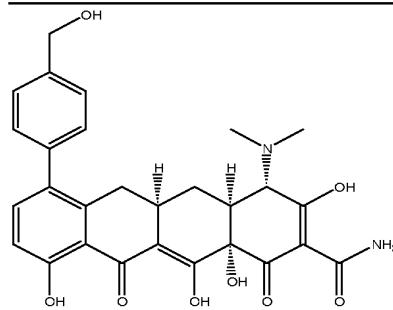
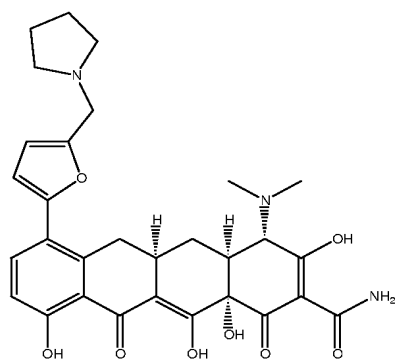
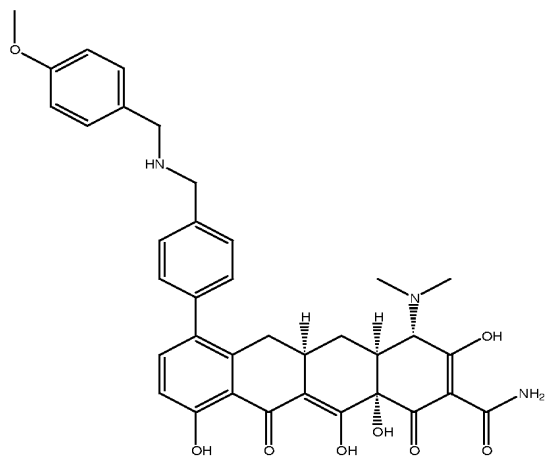
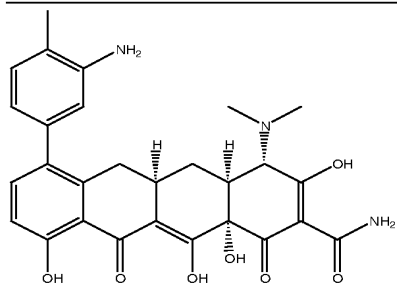
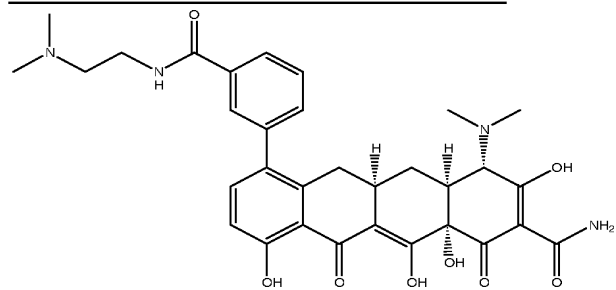
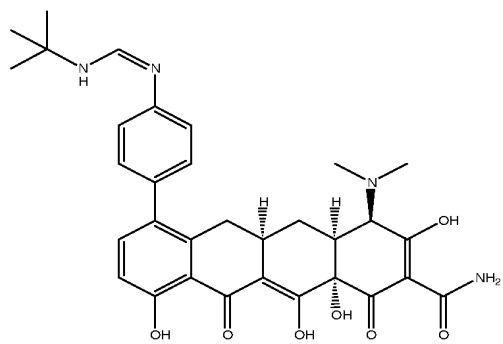
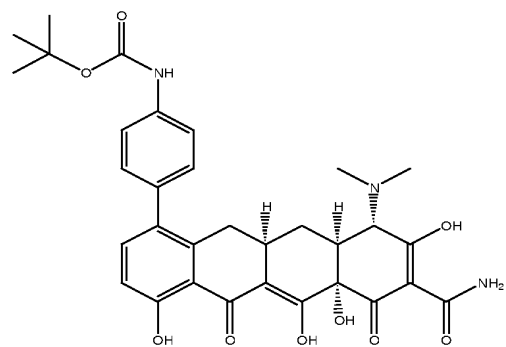
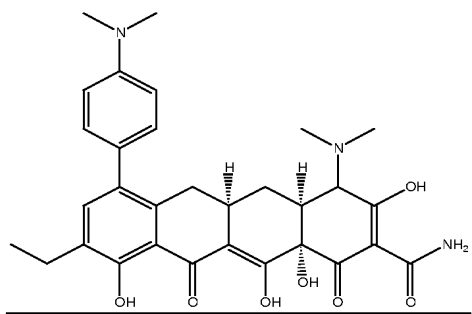


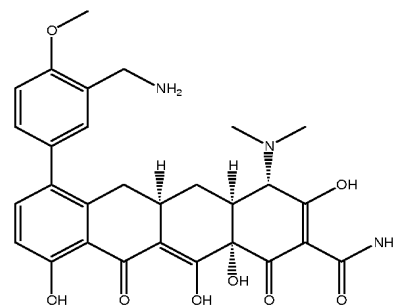
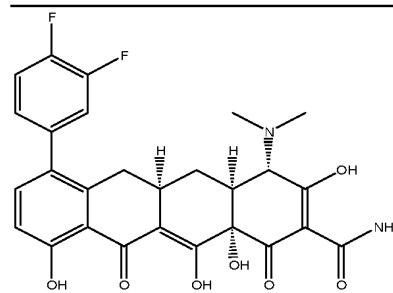
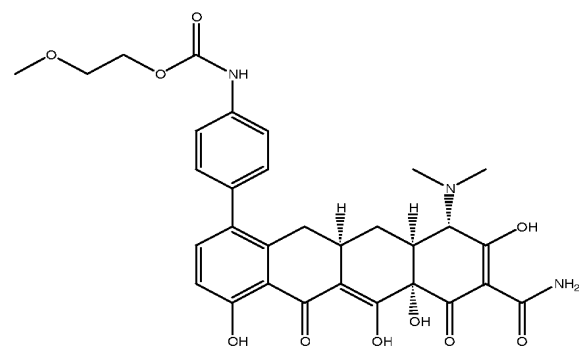
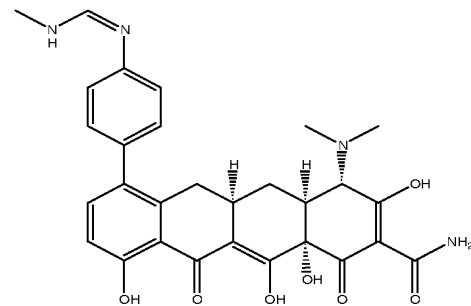
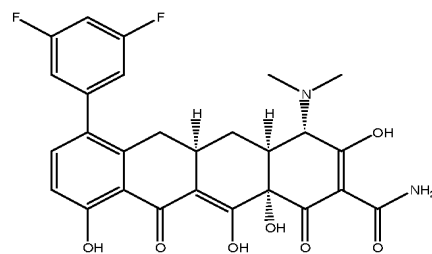
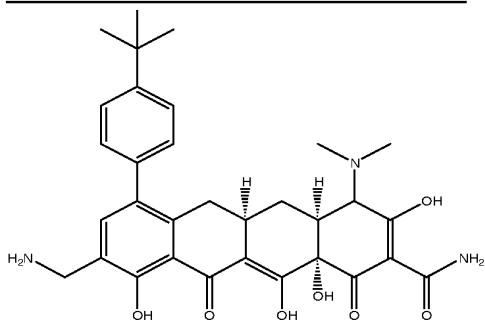
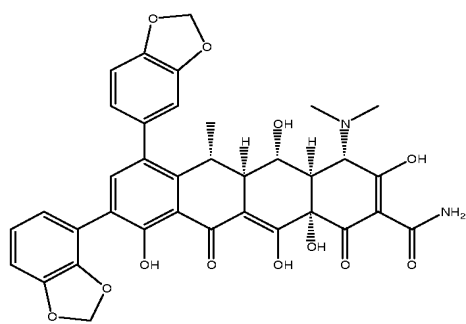
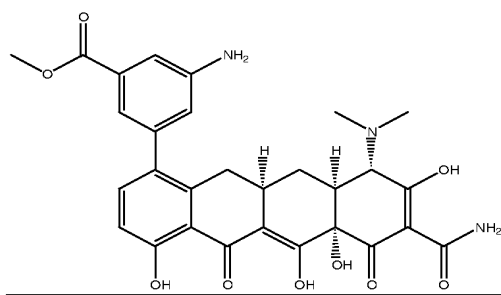
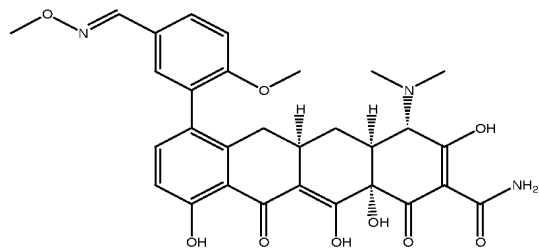
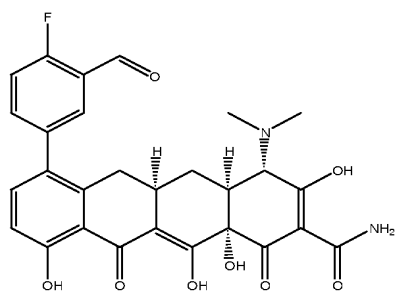


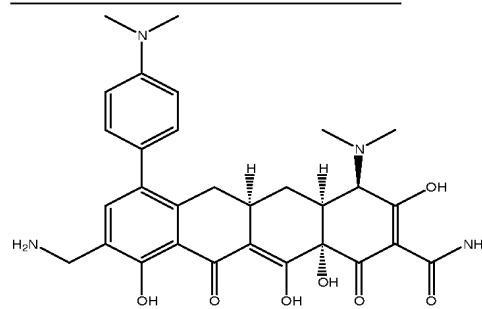
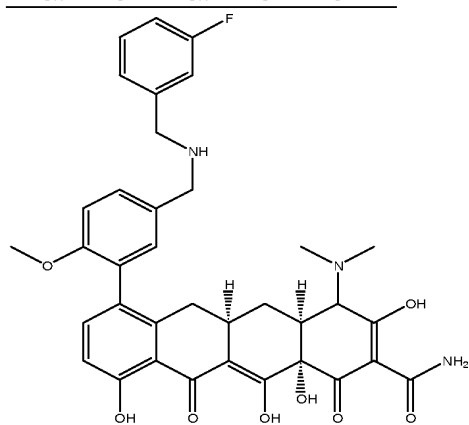
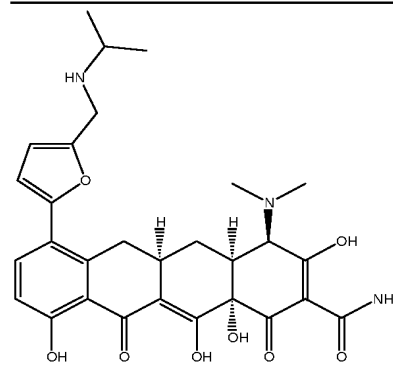
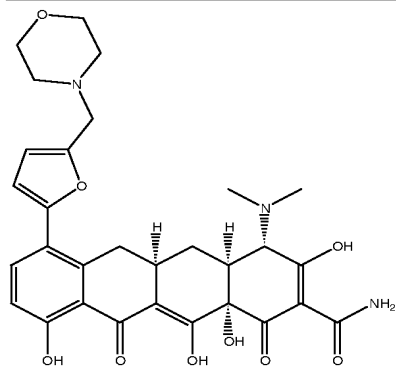
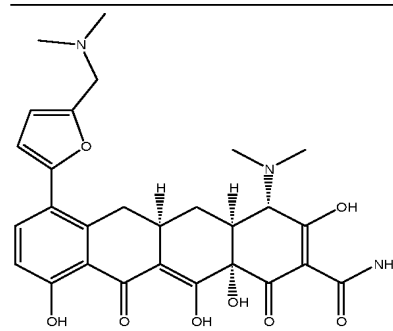
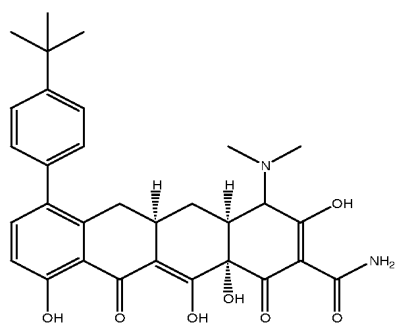
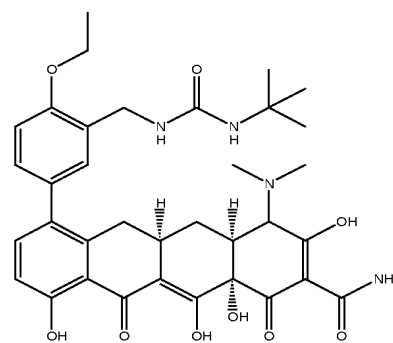
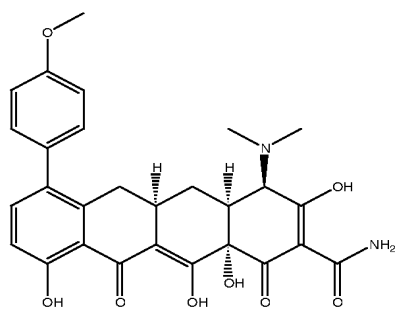


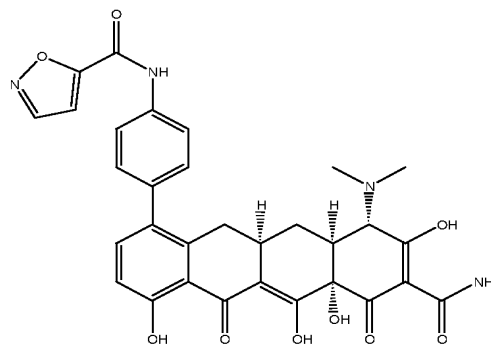
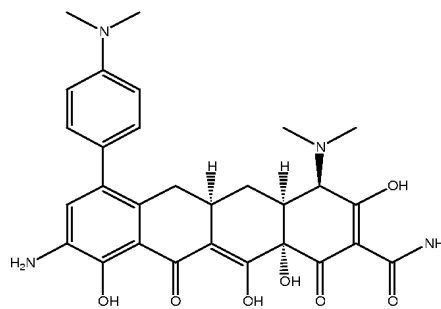
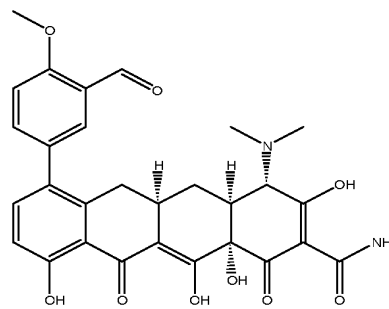
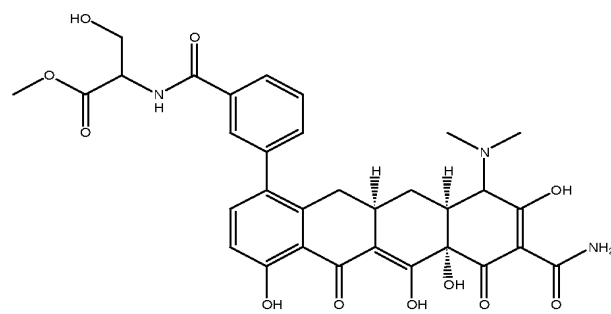
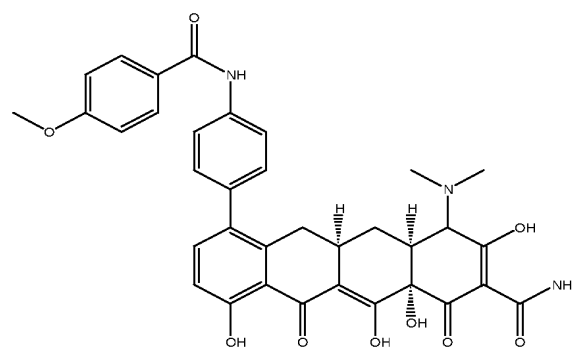
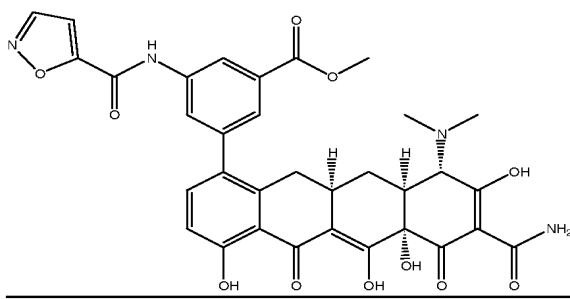
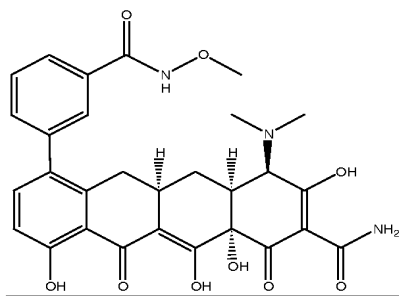
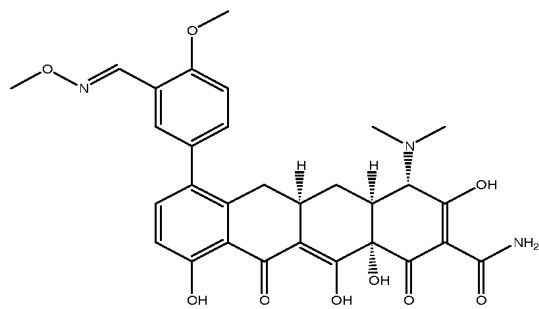
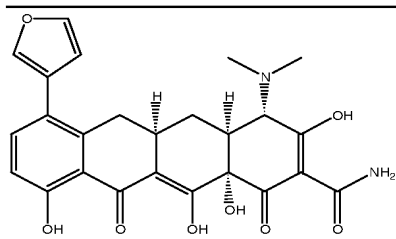
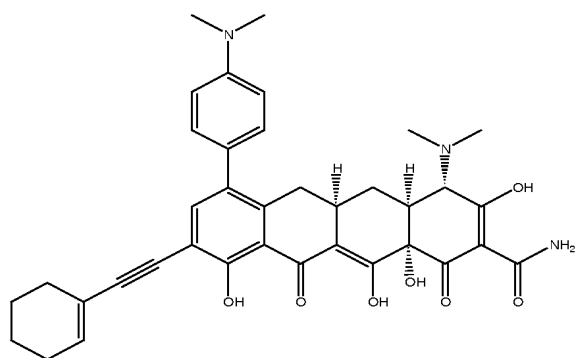


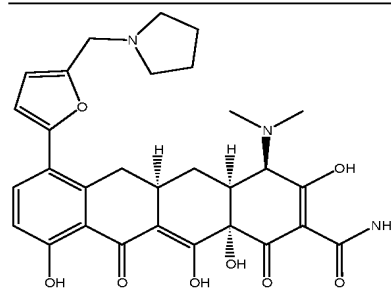
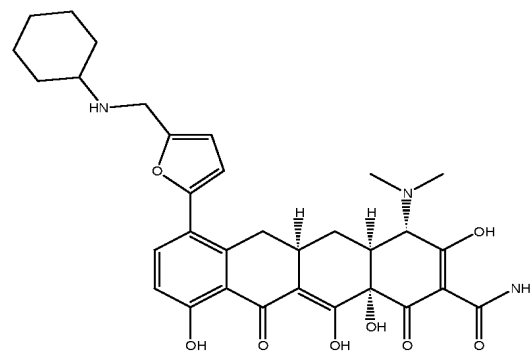
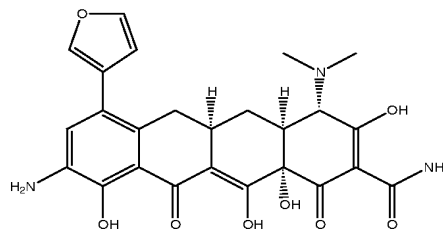
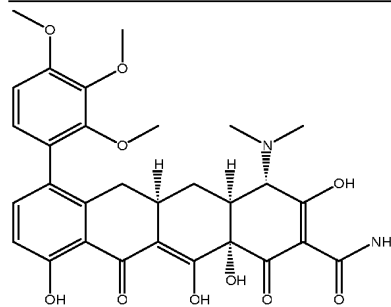
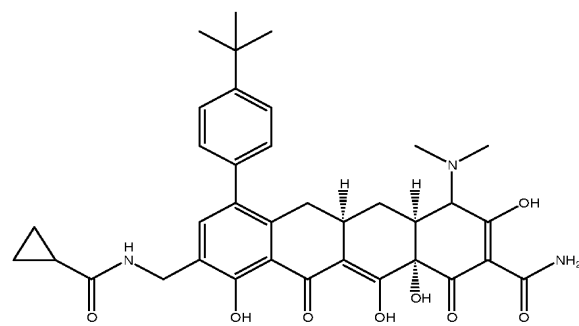
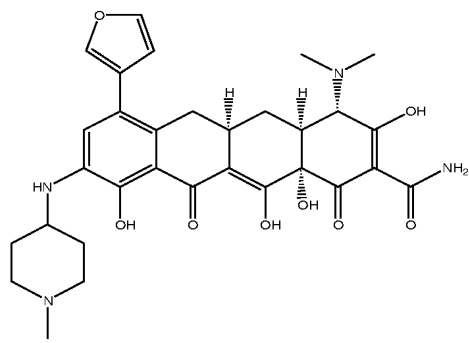
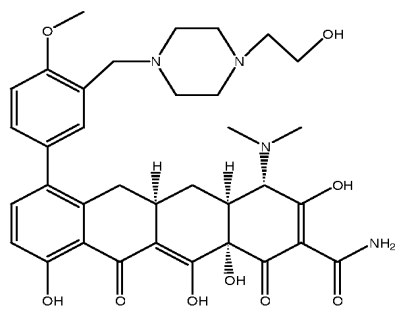
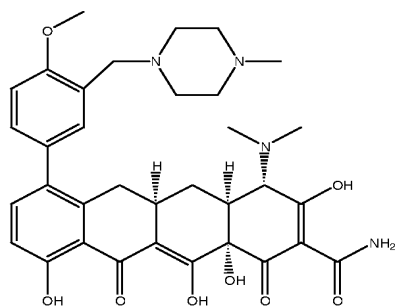
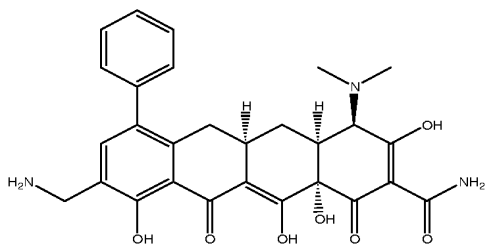
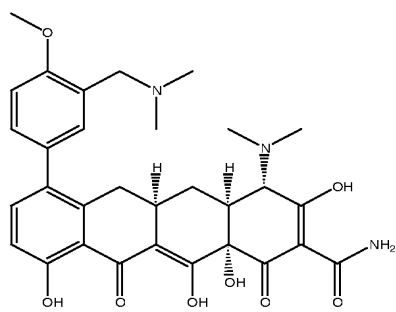


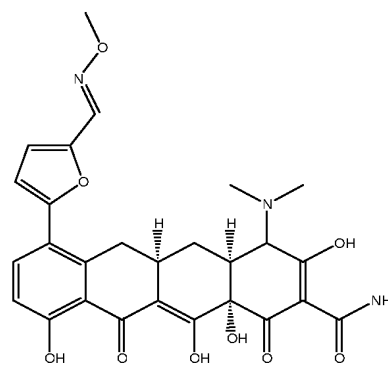
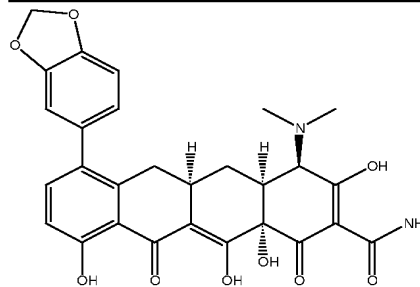
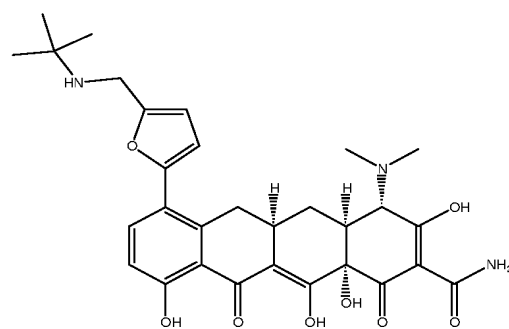
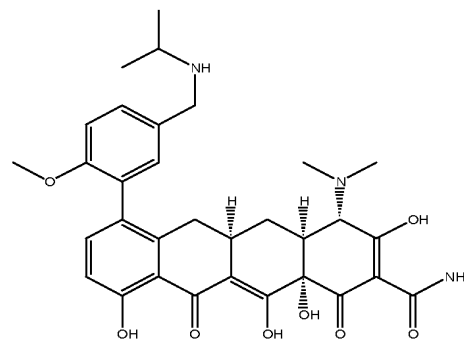
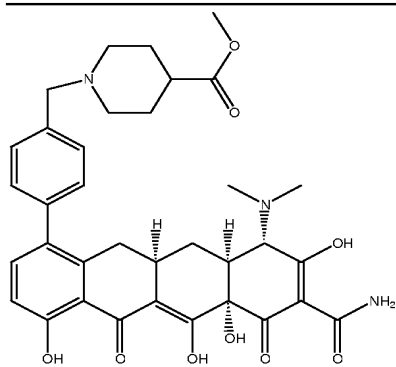
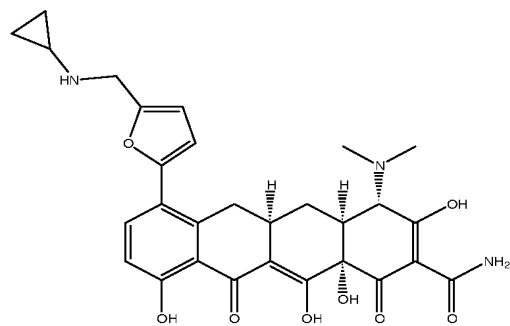
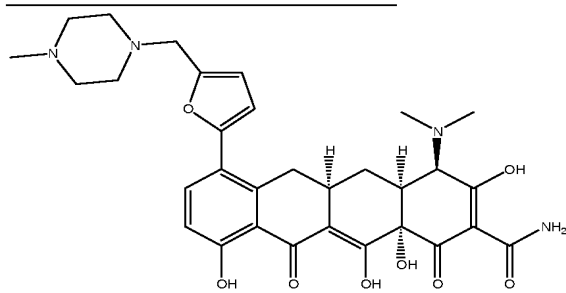
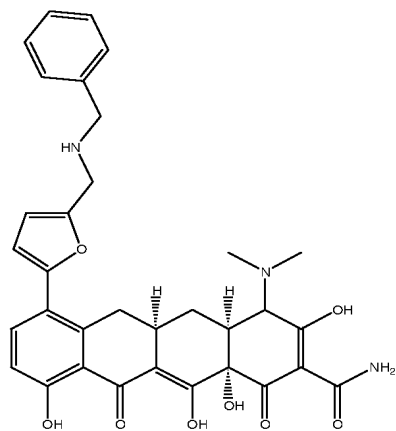


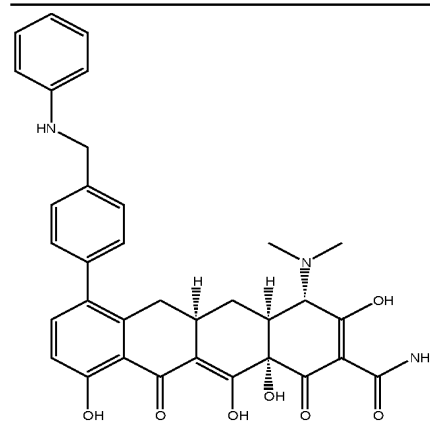
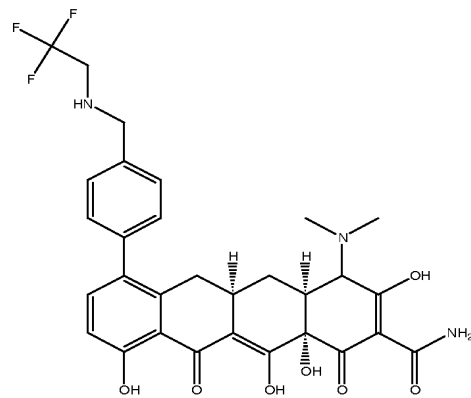
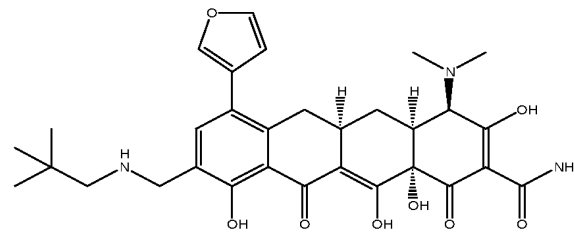
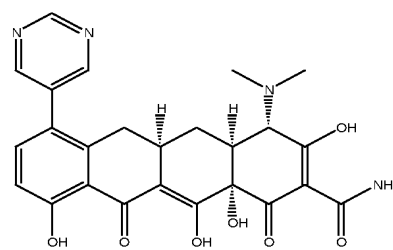
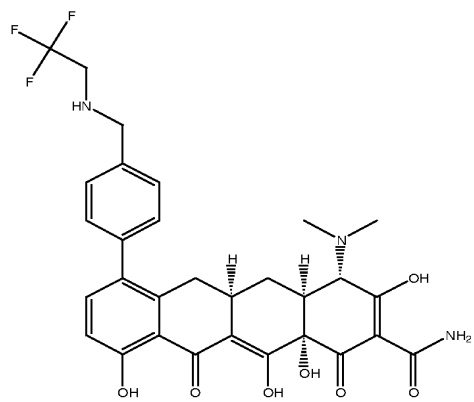
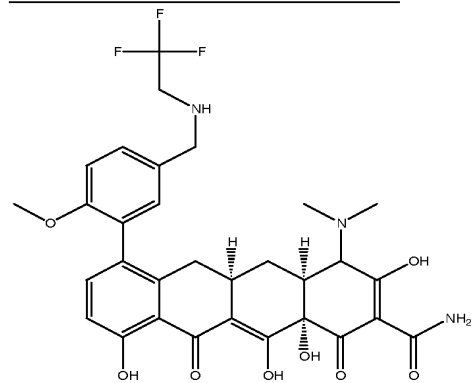
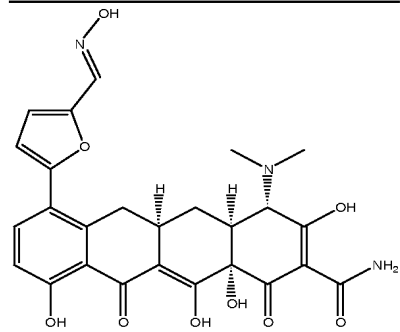
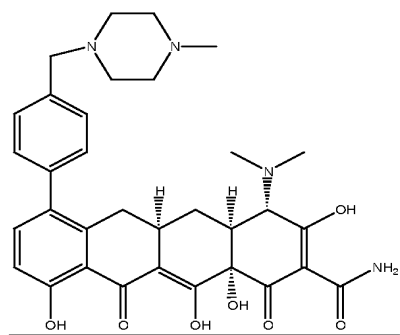


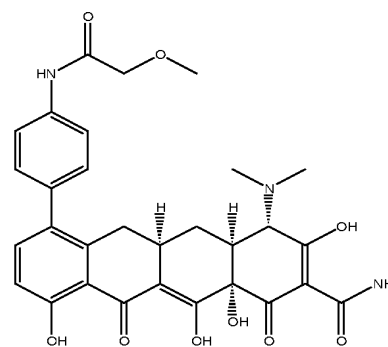
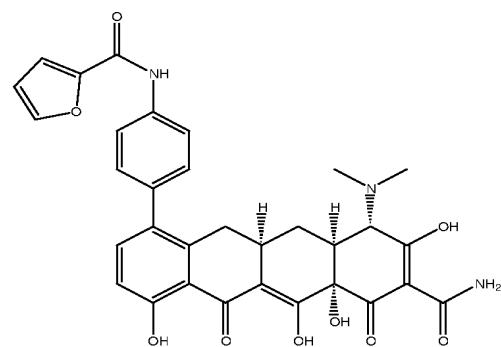
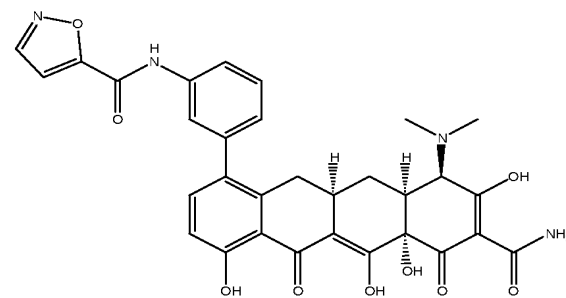
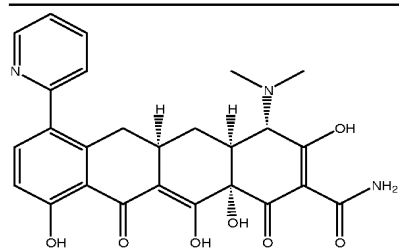
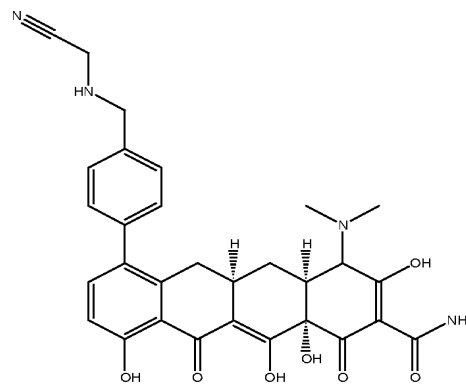
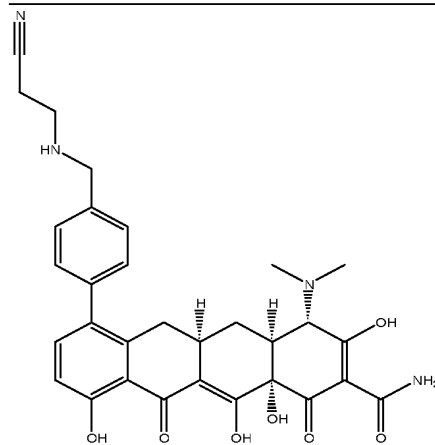
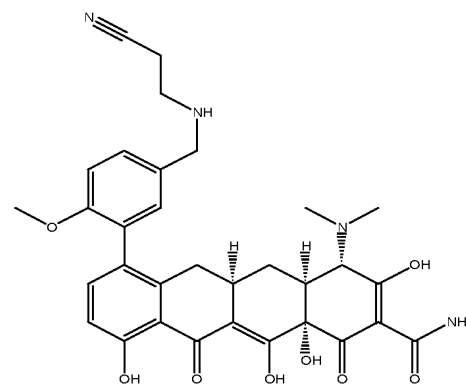
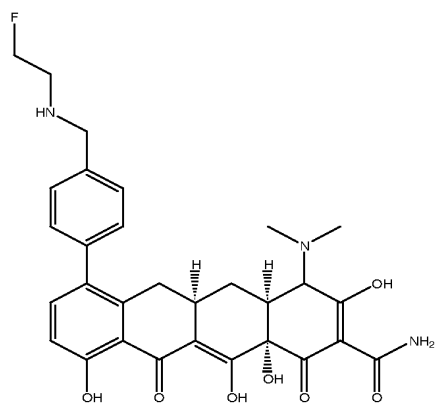


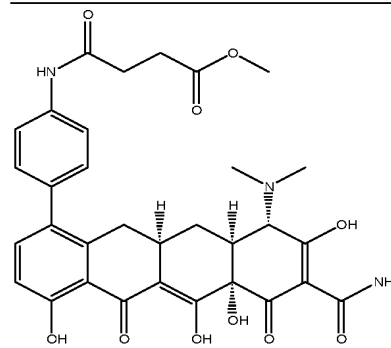
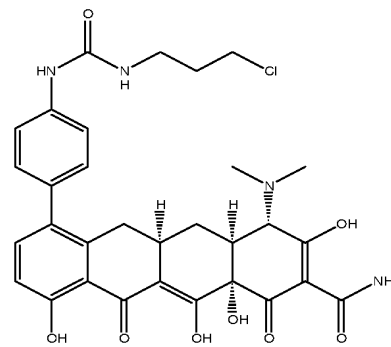
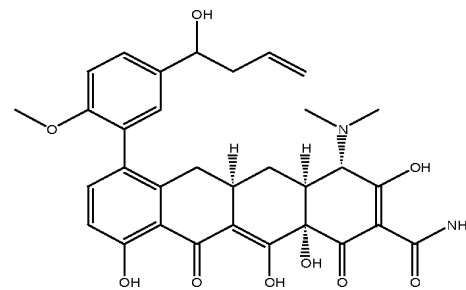
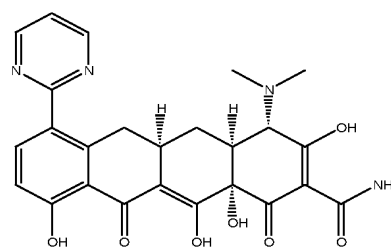


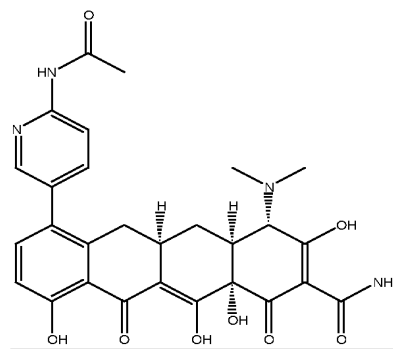
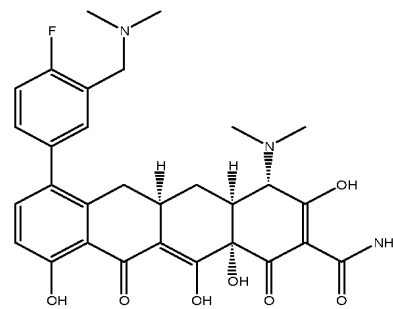
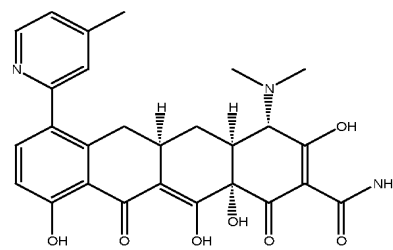
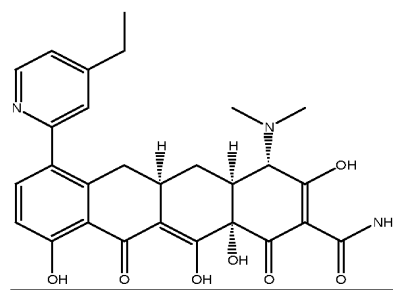
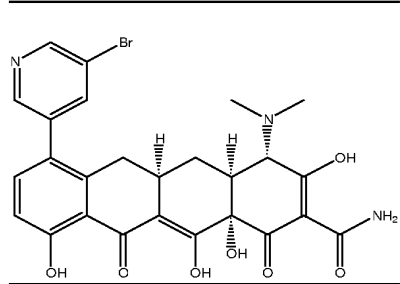
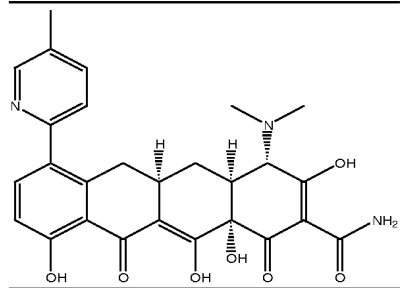
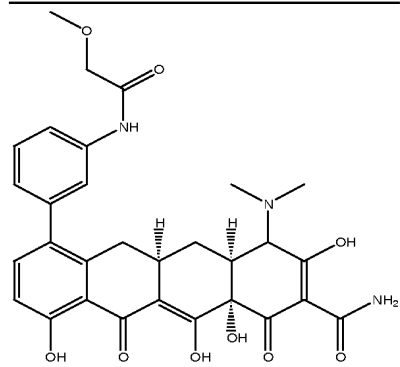
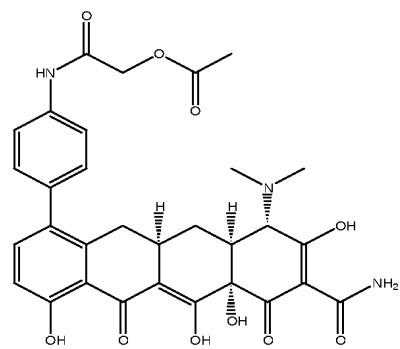




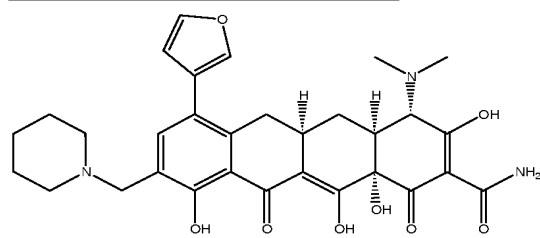
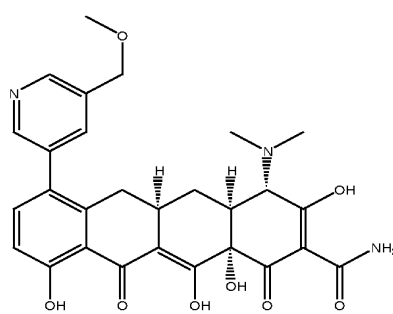
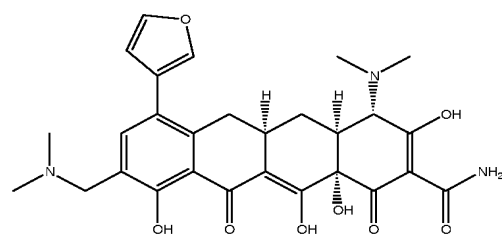
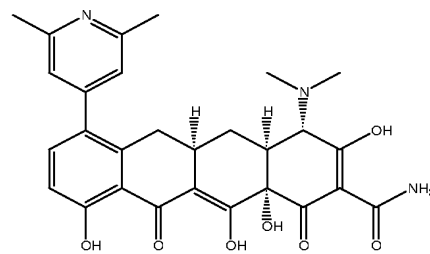


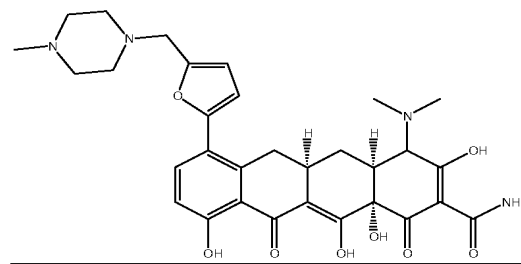
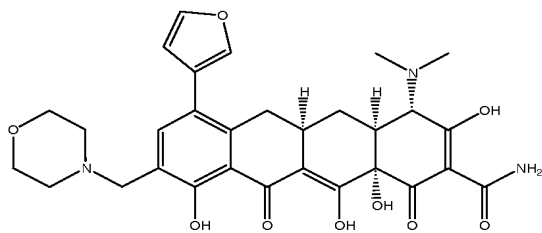
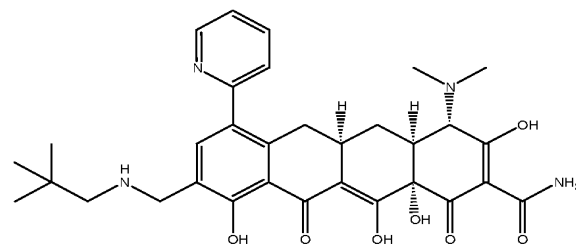
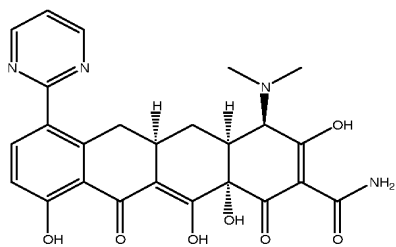
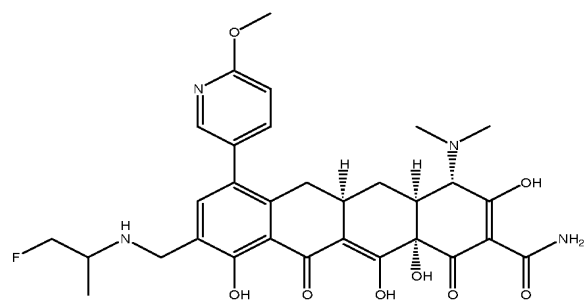
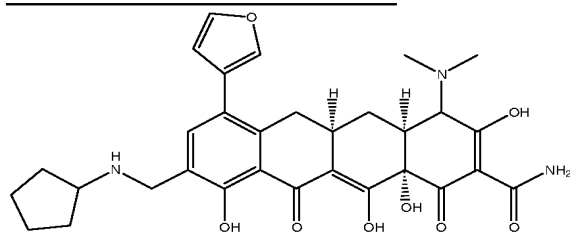
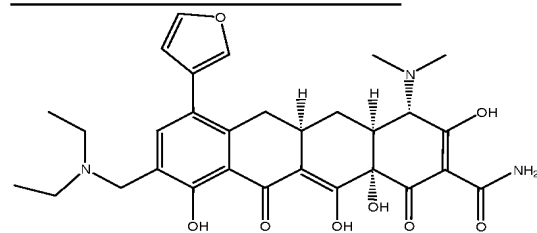
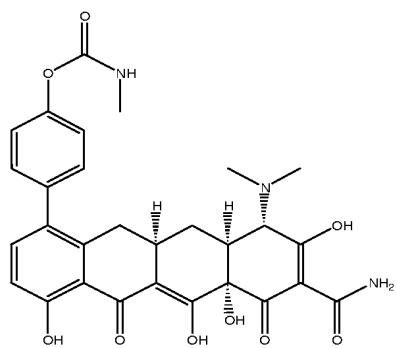
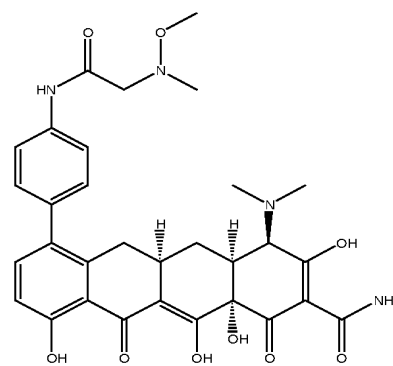
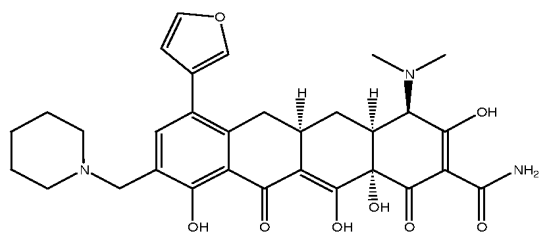


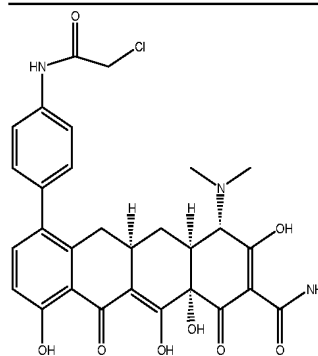
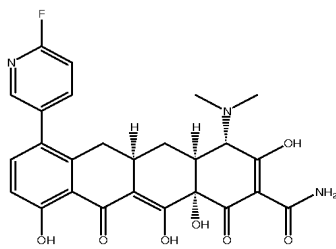
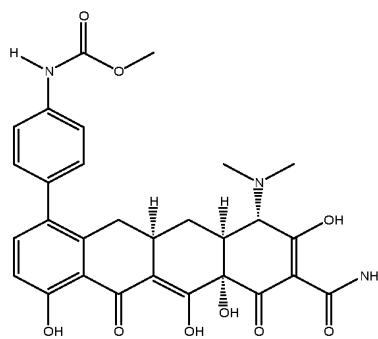
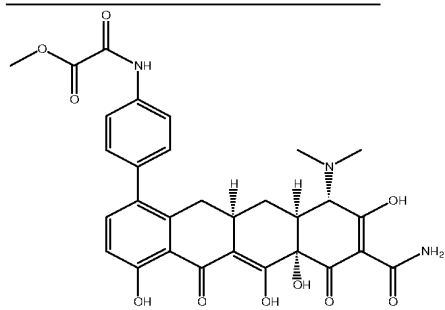
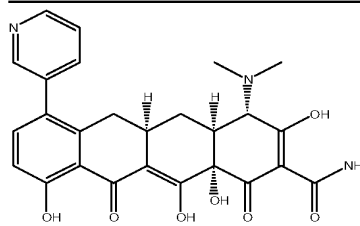
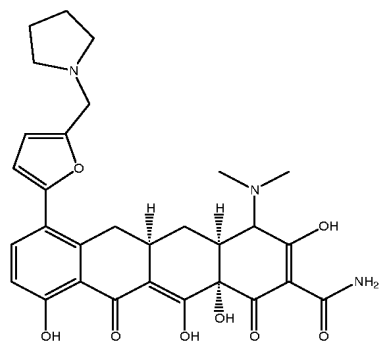
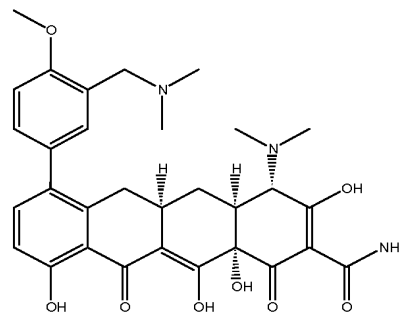
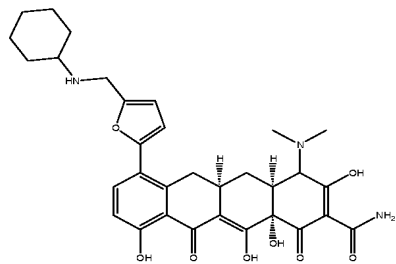
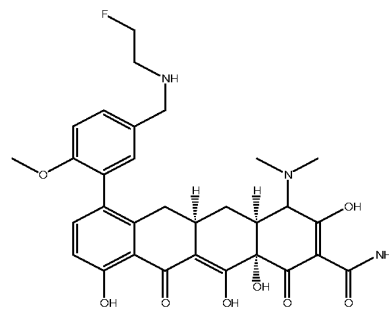
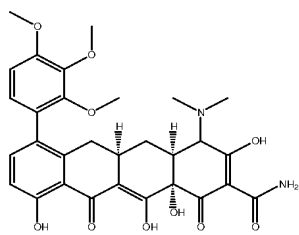


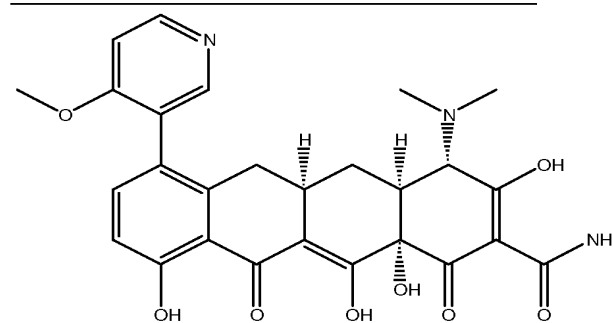
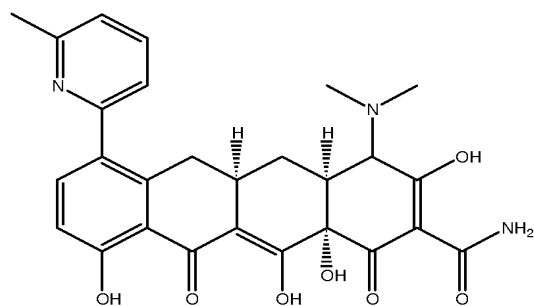
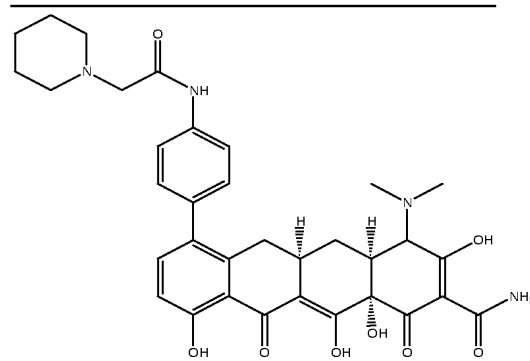
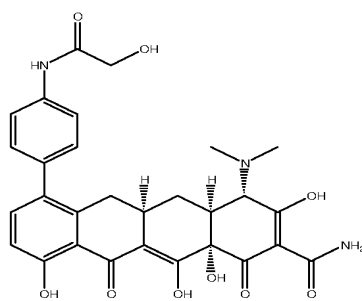
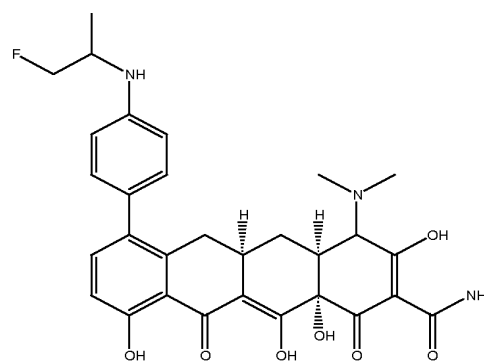
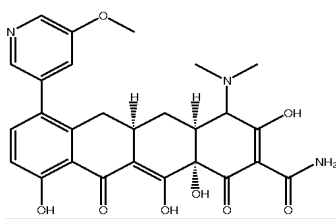
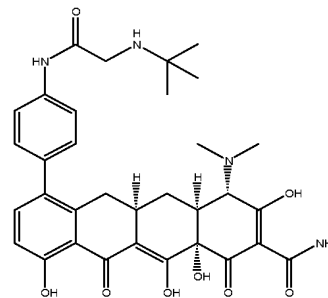
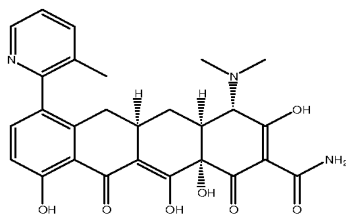
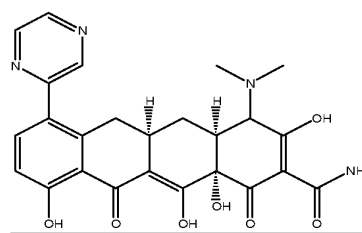
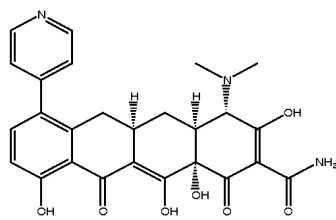


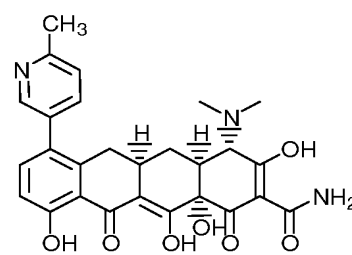
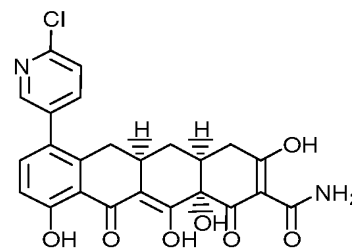
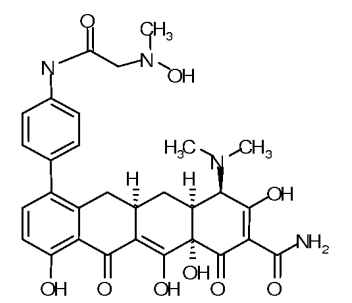
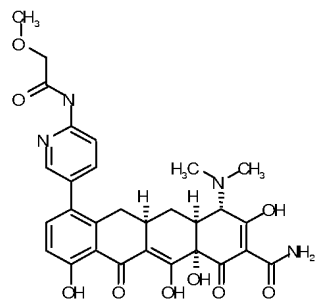
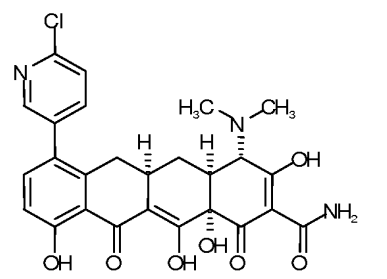
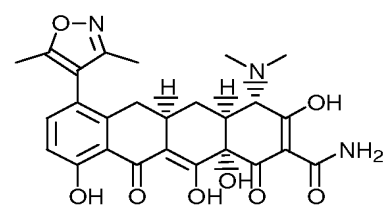
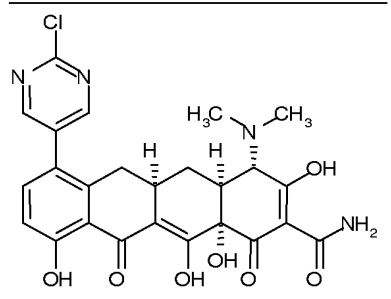
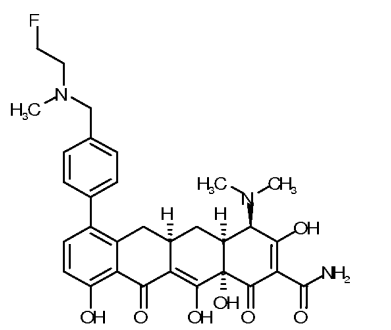
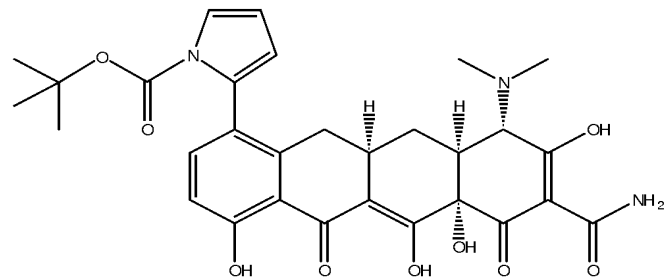
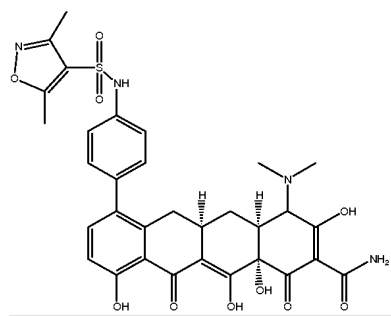
Examiner: Sabiha Naim Qazi
Group Art Unit: 1612

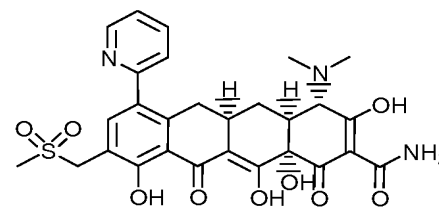
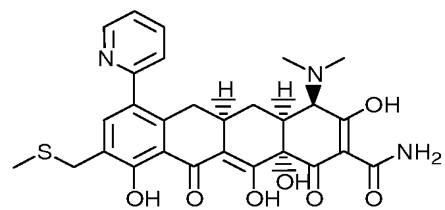
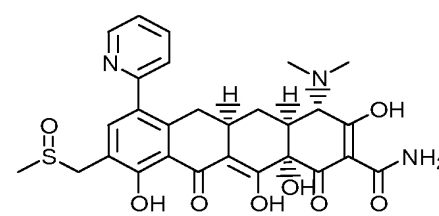
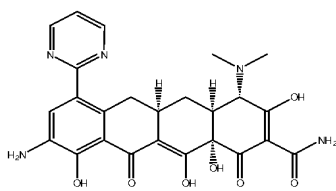
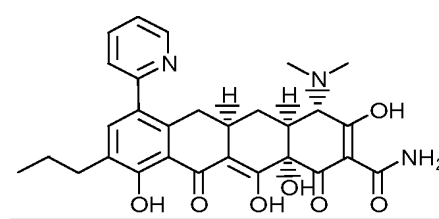
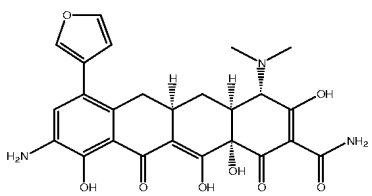
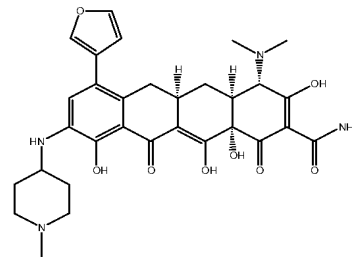
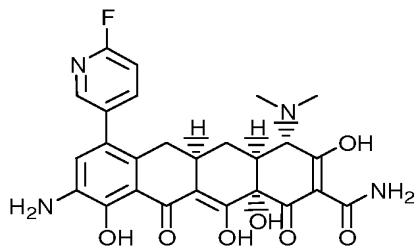
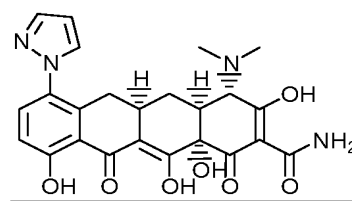
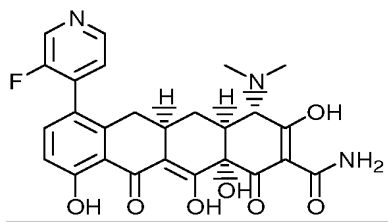


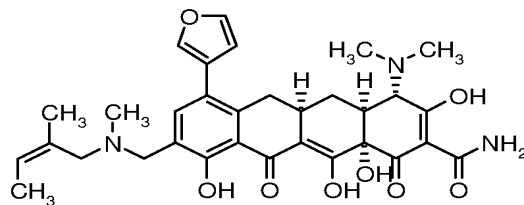
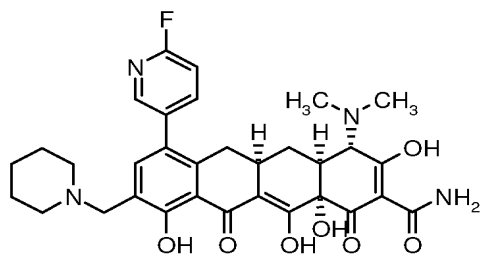
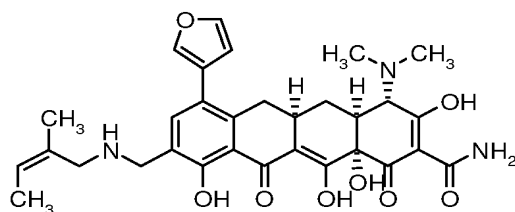
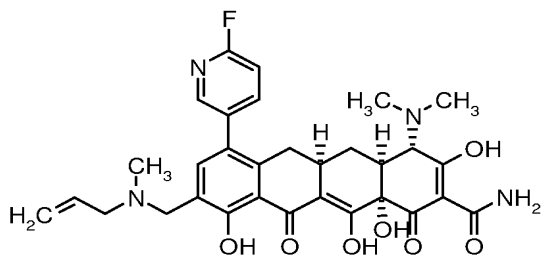
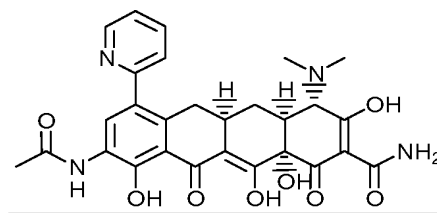
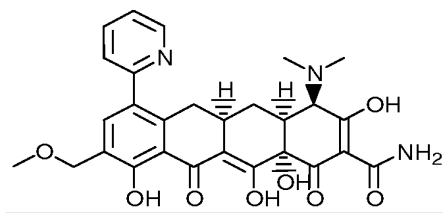
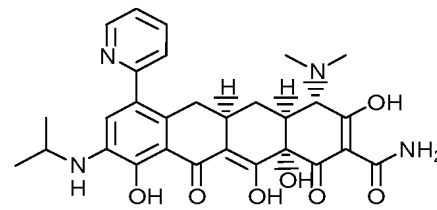
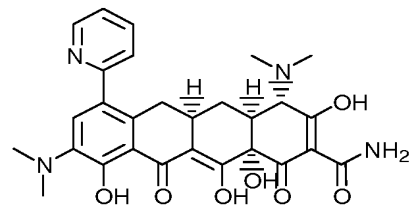
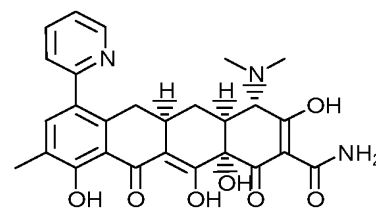
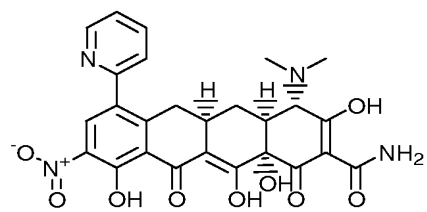


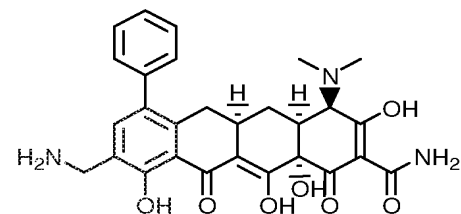
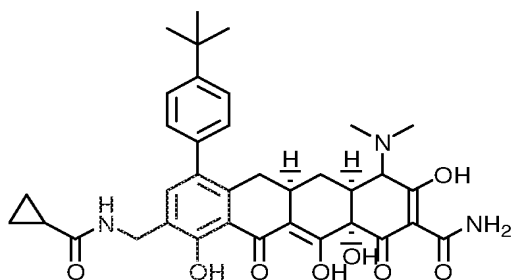
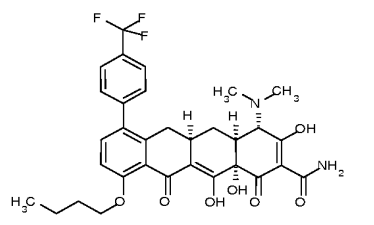
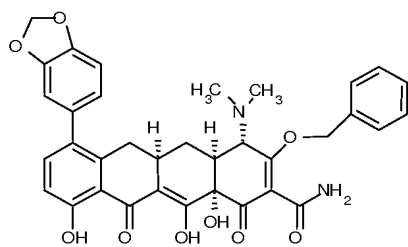
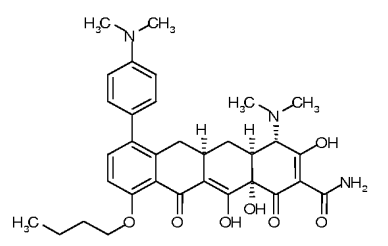
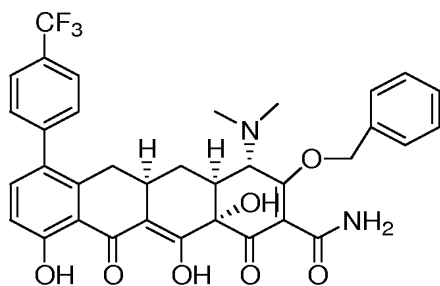
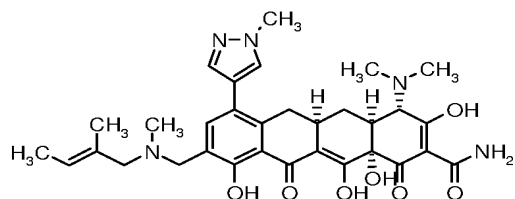
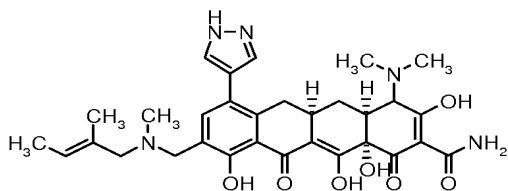
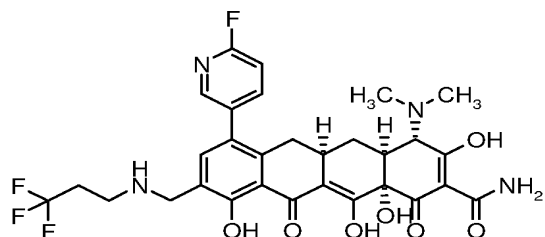
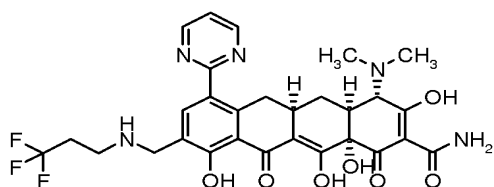


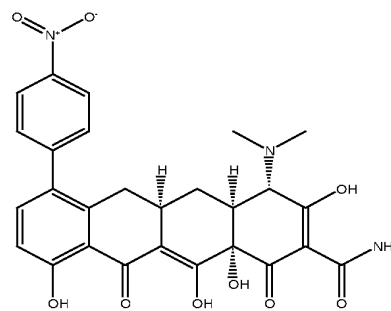
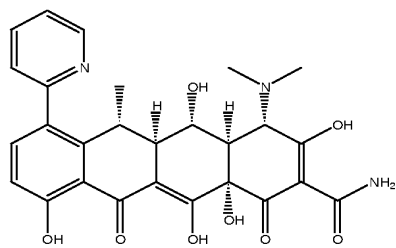
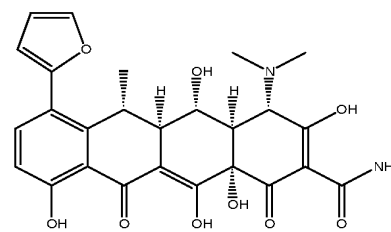
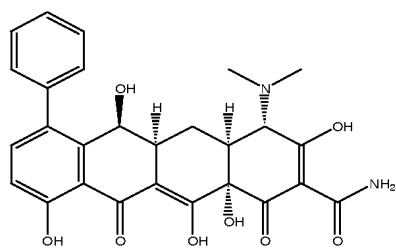
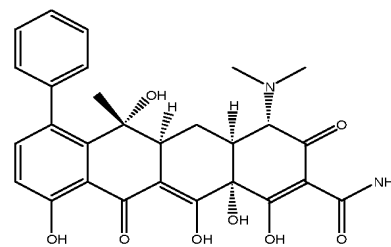
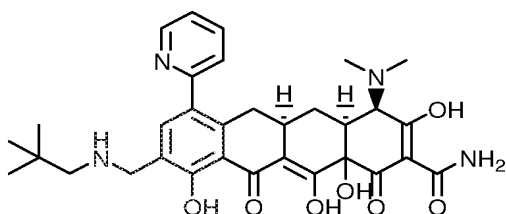
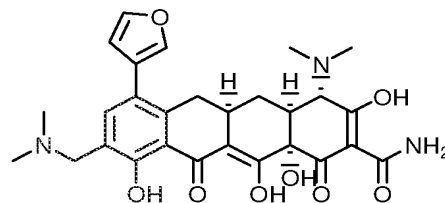
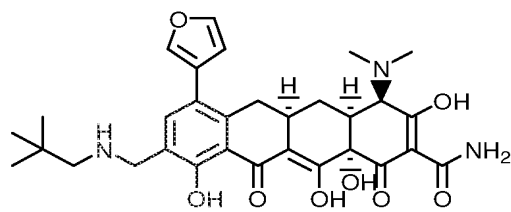
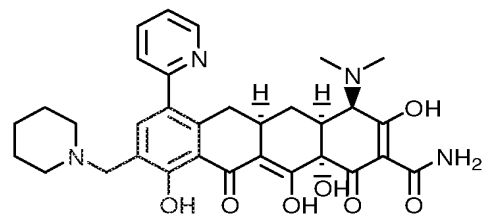
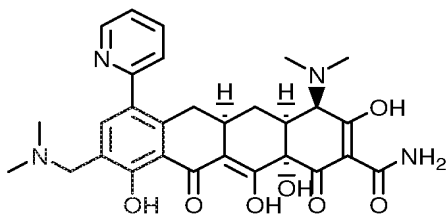


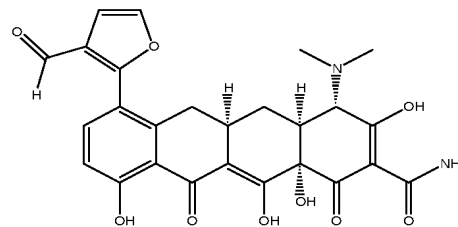
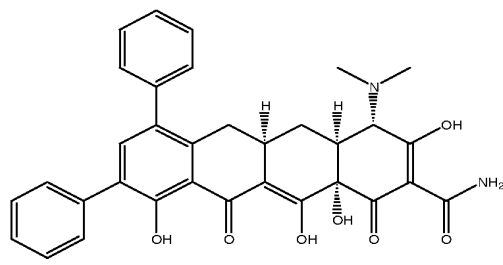
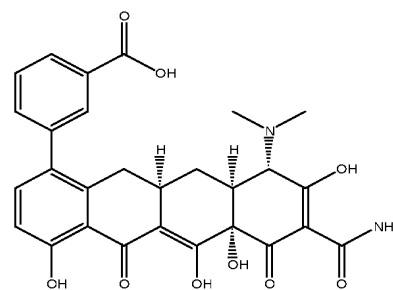
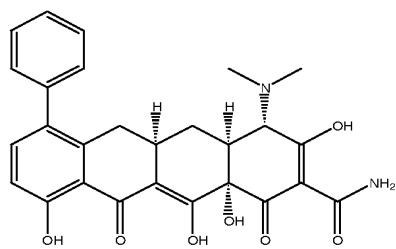
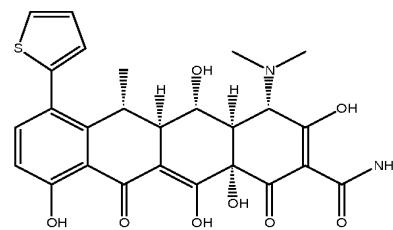
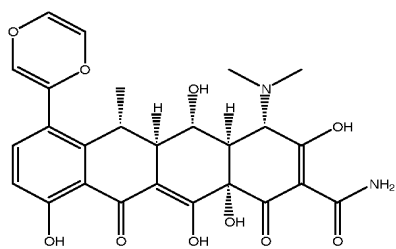
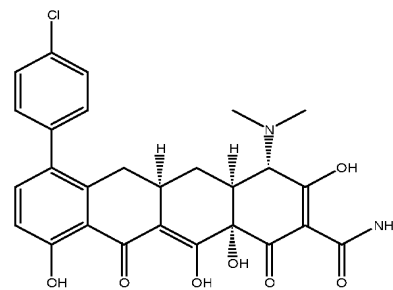
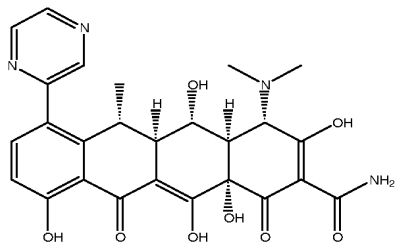
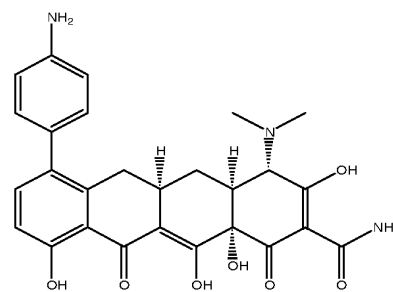
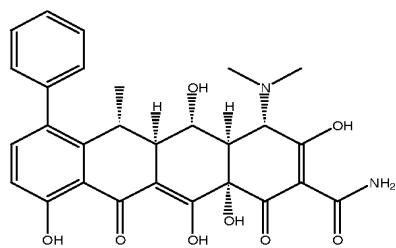


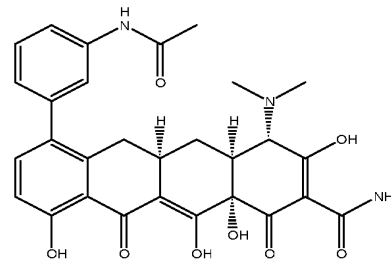
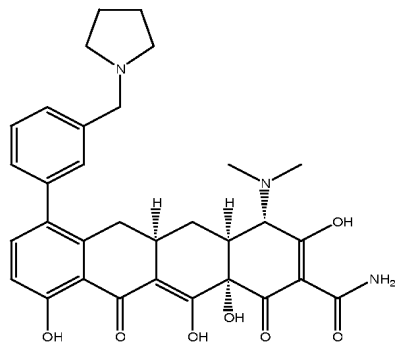
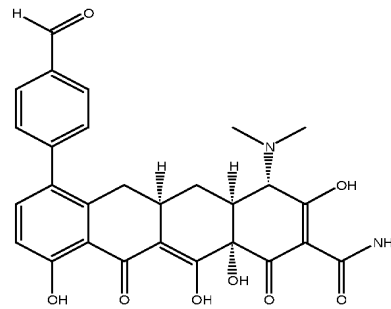
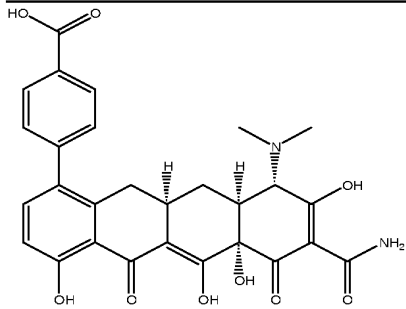
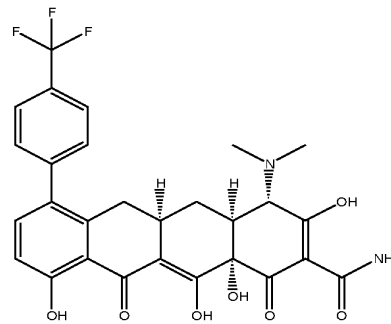
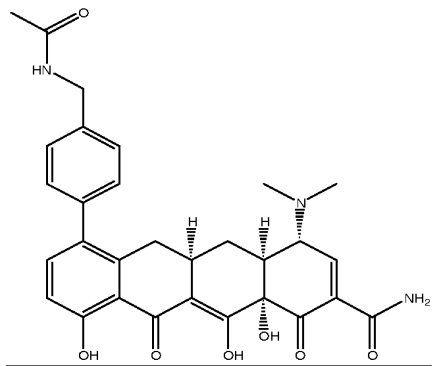
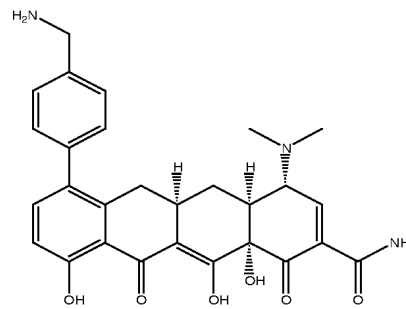
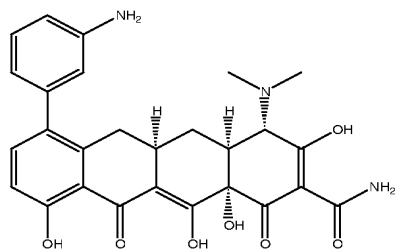


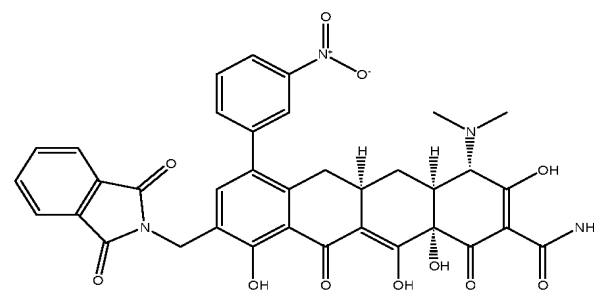
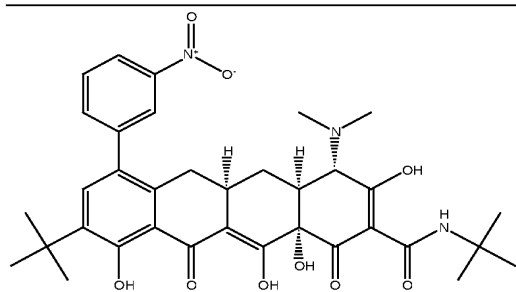
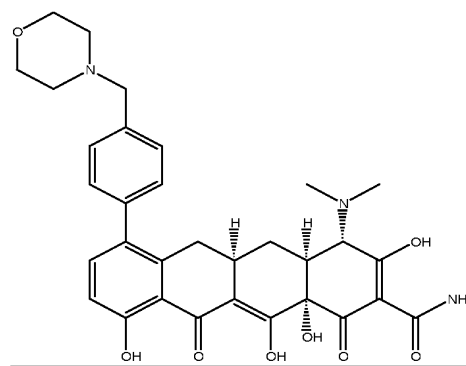
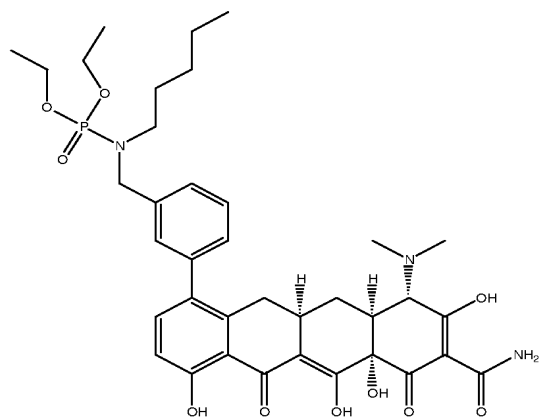
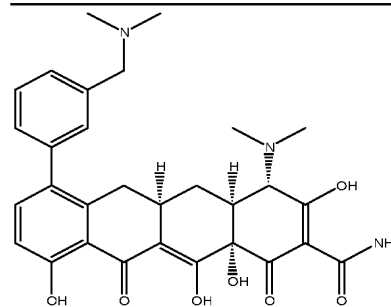
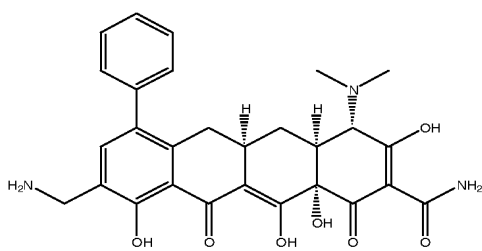
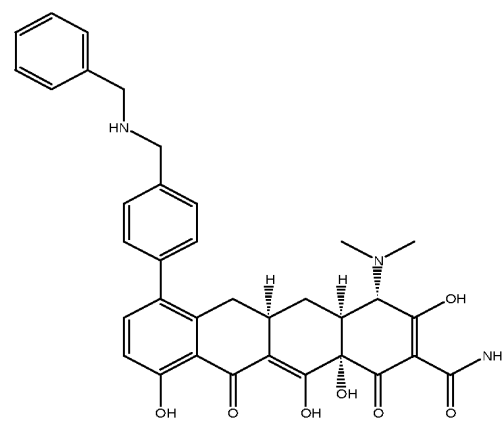
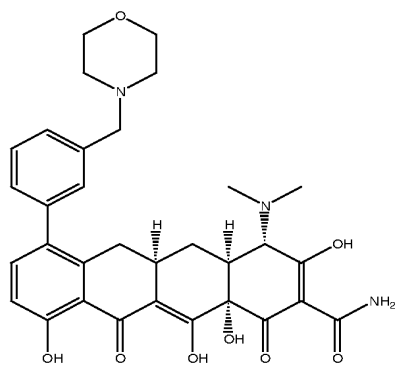


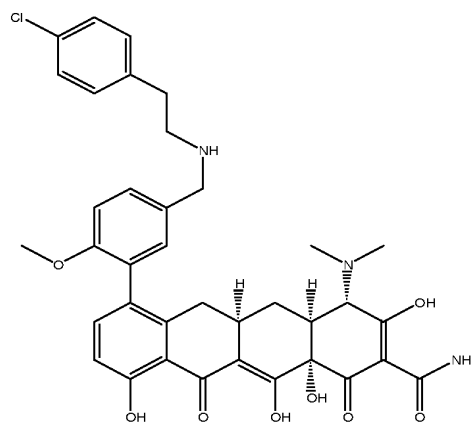
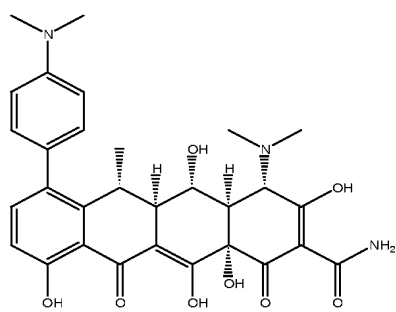
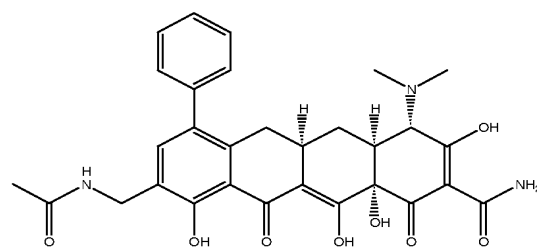
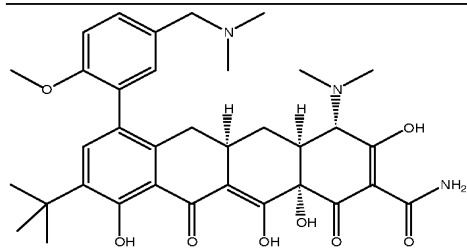
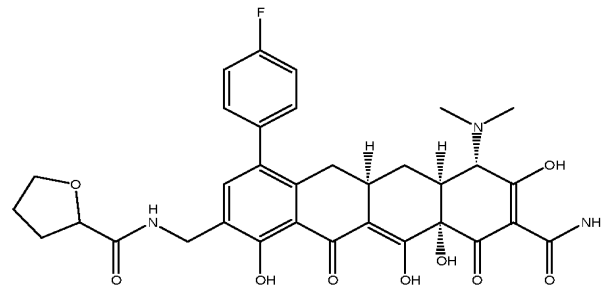
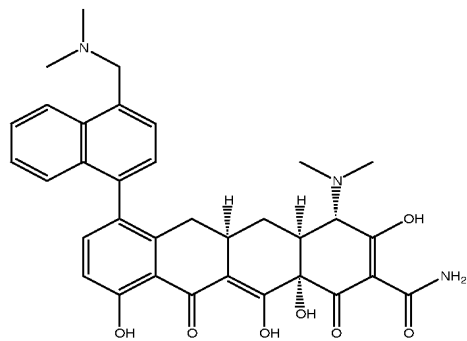
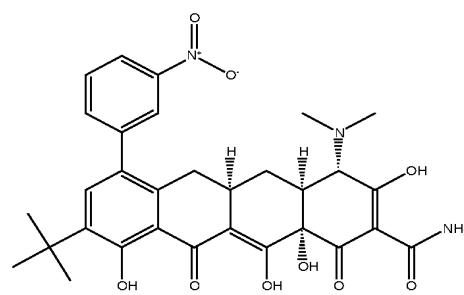
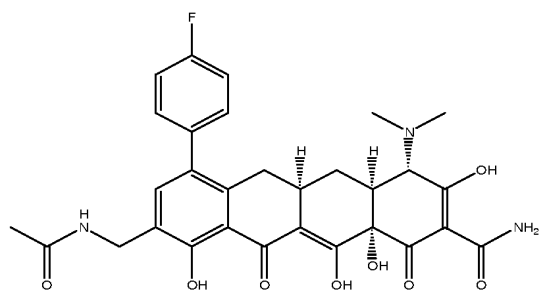


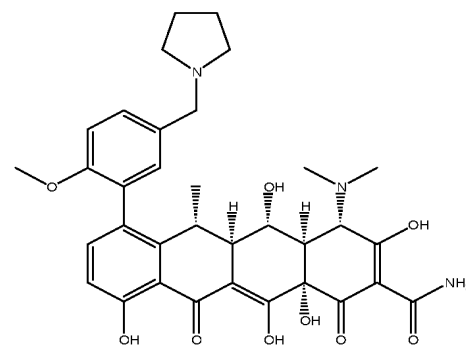
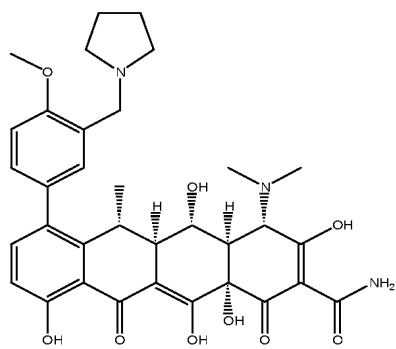
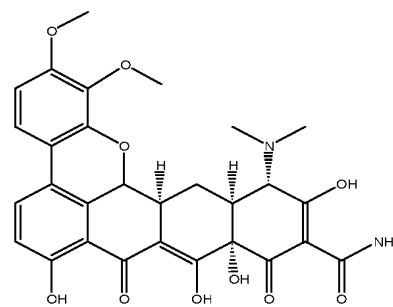
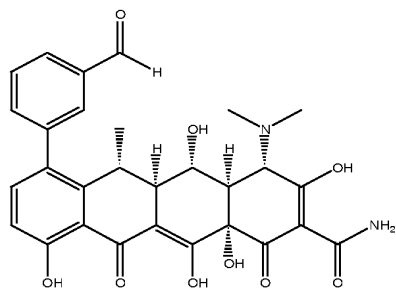
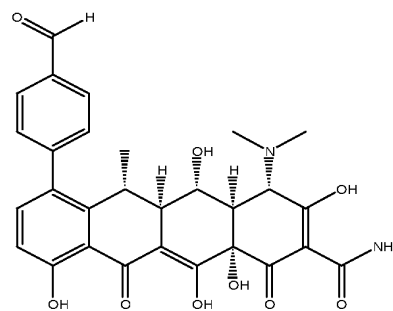
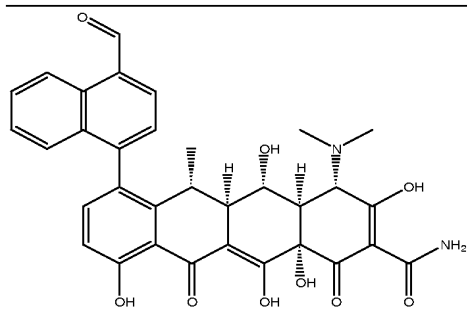
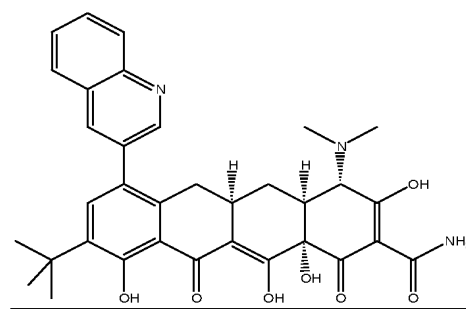
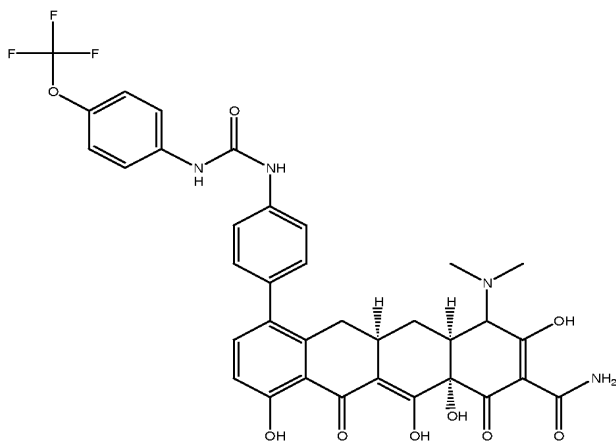


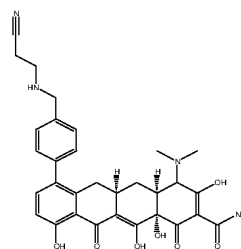
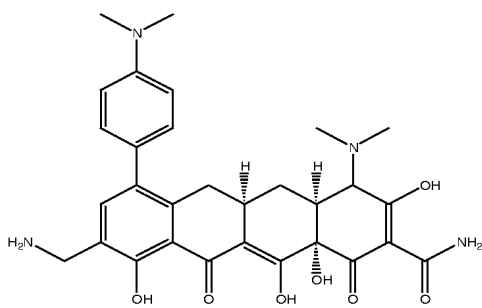
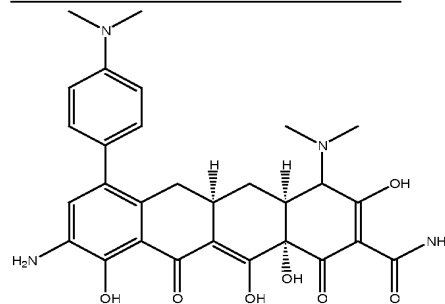
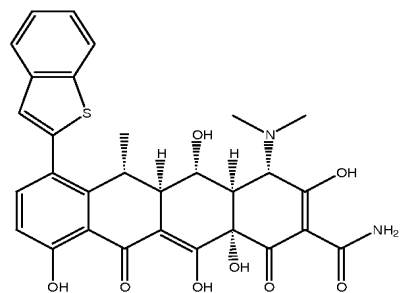
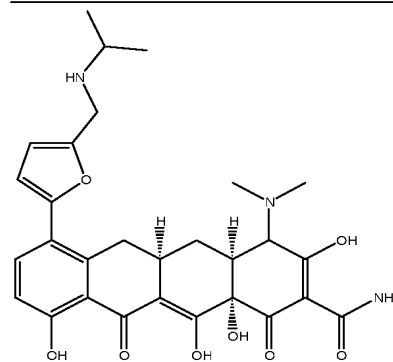
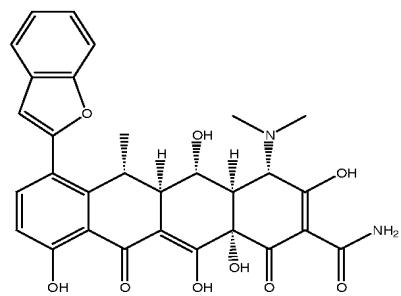
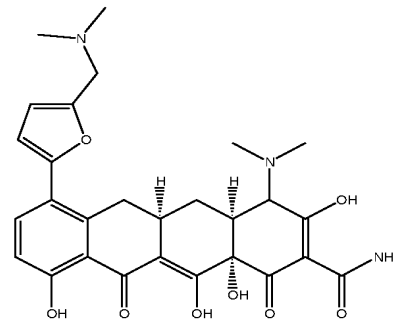
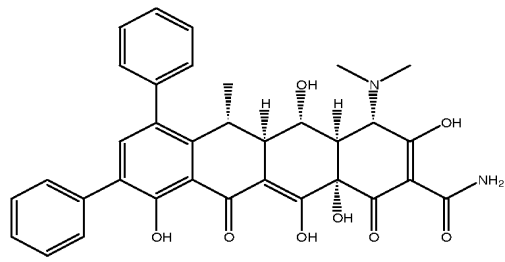
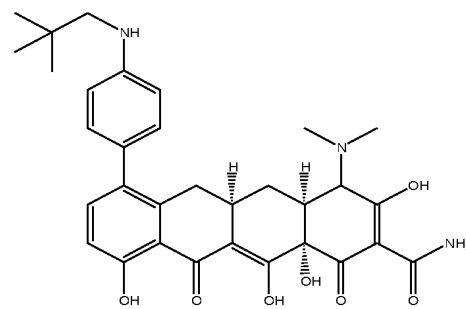
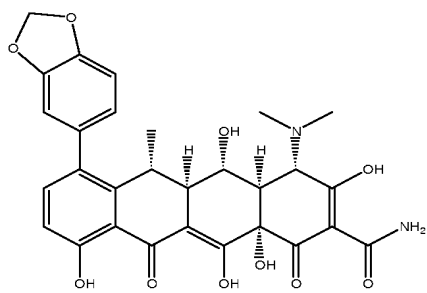


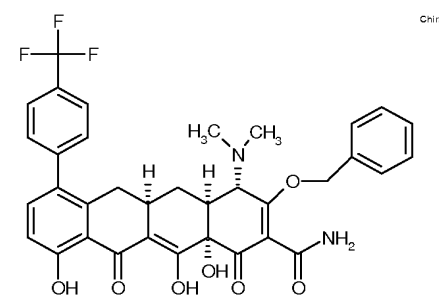
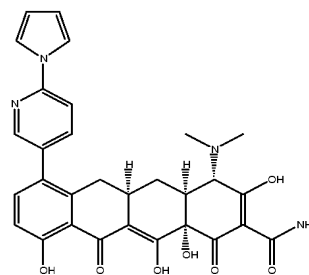
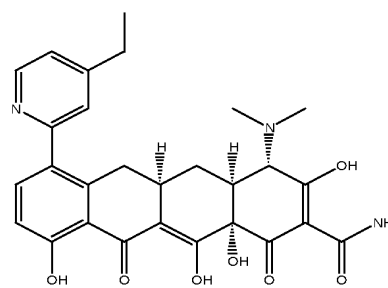
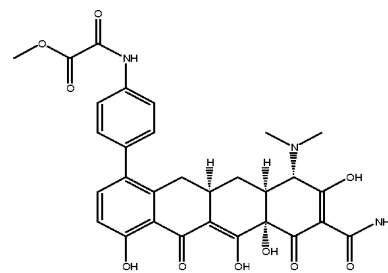
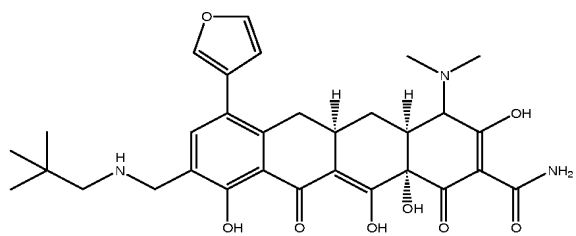
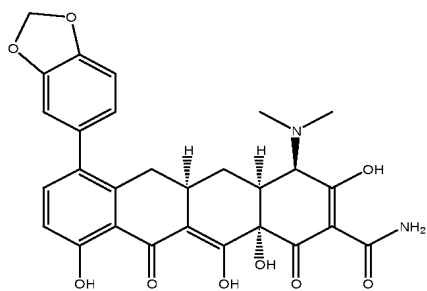
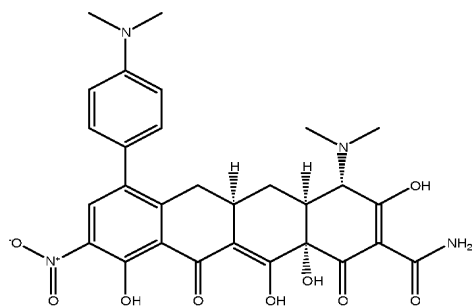
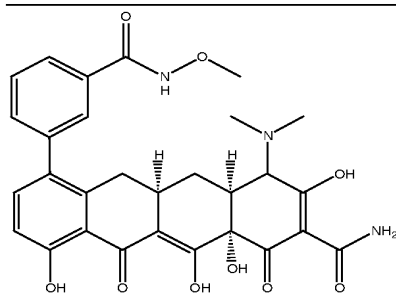
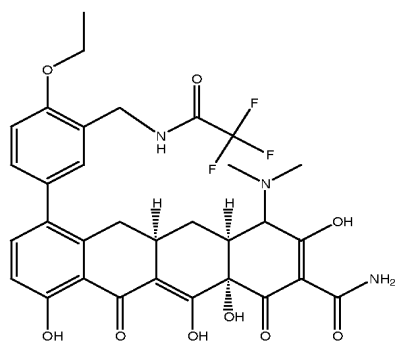




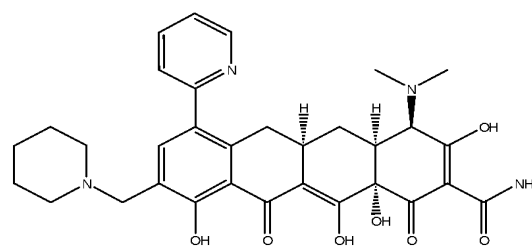


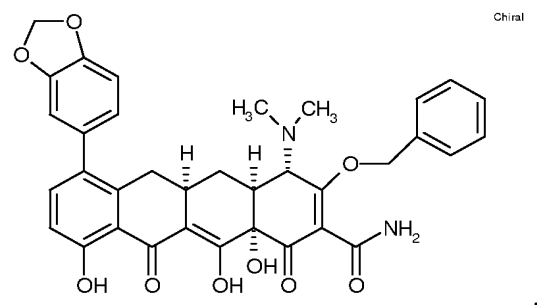
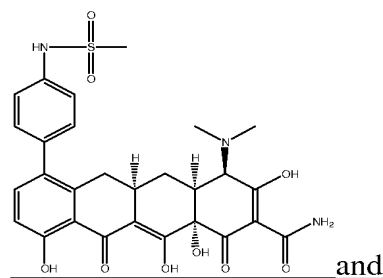
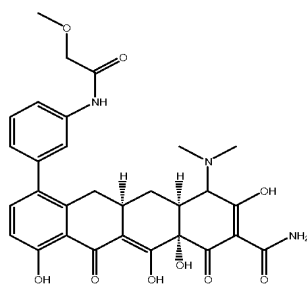
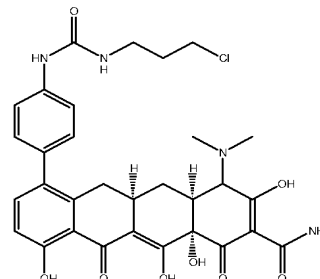
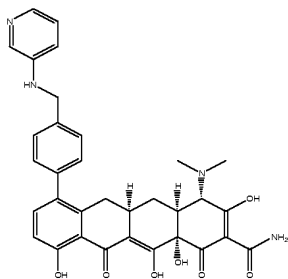
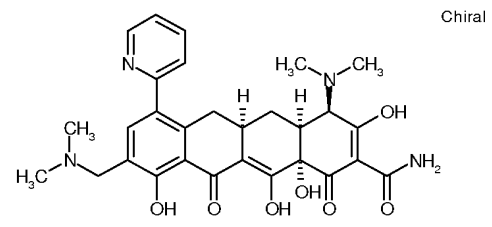
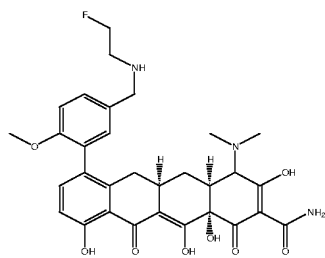






Chiral





51. (Original) The method of claim 1, wherein said subject is a human.

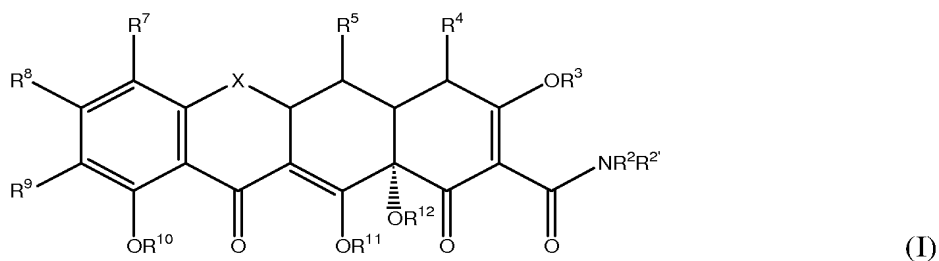
52. (Original) The method of claim 1, wherein said substituted tetracycline compound is has anti-microbial gram positive activity.

53. (Original) The method of claim 52, wherein said anti-microbial gram positive activity is greater than about 0.05 µg/ml.

54. **(Original)** The method of claim 53, wherein said anti-microbial gram positive activity is greater than about 5 µg/ml.
55. **(Original)** The method of claim 1, wherein said substituted tetracycline compound in non-antibacterial.
56. **(Original)** The method of claim 1, wherein said substituted tetracycline compound has a cytotoxicity of 25 µg/ml or greater.
57. **(Original)** The method of claim 1, wherein said substituted tetracycline compound has a MIC of 150 nM or less.
58. **(Original)** The method of claim 57, wherein said substituted tetracycline compound has a MIC of 50 nM or less.
59. **(Original)** The method of claim 58, wherein said substituted tetracycline compound has a MIC of 10 nM or less.
60. **(Original)** The method of claim 59, wherein said substituted tetracycline compound has an MIC or 5 nM or less.
61. **(Original)** The method of claim 1, wherein said malaria is caused by a plasmodium protozoan selected from the group consisting of: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*.
62. **(Original)** The method of claim 1, wherein said malaria is resistant to one or more anti-malarial compounds selected from the group consisting of: proguanil, chlorproguanil, trimethoprim, chloroquine, mefloquine, lumefantrine, atovaquone, pyrimethamine-sulfadoxine, pyrimethamine-dapsone, halofantrine, quinine, quinidine, amodiaquine, amopyroquine, sulphonamides, artemisinin, arteflene, artemether, artesunate, primaquine, pyronaridine, proguanil, and 1,16-hexadecamethylenebis(N-methylpyrrolidinium) dibromide.
- 63 – 65. **(Cancelled)**
66. **(Currently Amended)** ~~The method of claim 65,~~ The method of claim 1, further comprising administering an ~~wherein said anti-malarial compound is~~

selected from the group consisting of: proguanil, chlorproguanil, trimethoprim, chloroquine, mefloquine, lumefantrine, atovaquone, pyrimethamine-sulfadoxine, pyrimethamine-dapsone, halofantrine, quinine, quinidine, amodiaquine, amopyroquine, sulphonamides, artemisinin, arteflene, artemether, artesunate, primaquine, pyronaridine, 1,16-hexadecamethylenebis(N-methylpyrrolidinium)dibromide, and combinations thereof.

67. **(Previously Presented)** A method for increasing the antimalarial activity of an antimalarial compound, comprising administering said antimalarial compound in combination with an effective amount of a substituted tetracycline compound, such that the antimalarial activity of said antimalarial compound is increased, wherein said tetracycline compound is of formula I:



wherein:

X is CR^{6'}R⁶;

R², R^{2'}, R^{4'}, and R^{4''} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ is NR^{4'}R^{4''}, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R³, R¹¹ and R¹² are each hydrogen, or a pro-drug moiety;

R¹⁰ is hydrogen, or a prodrug moiety;

R⁵ is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R⁶ and R^{6'} are independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

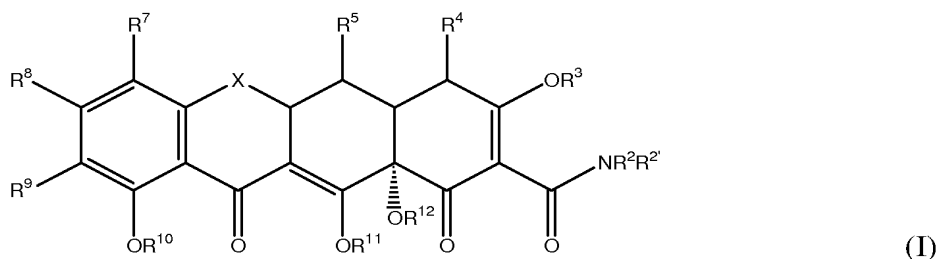
R⁷ is aryl;

R⁹ is hydrogen;

R⁸ is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and pharmaceutically acceptable salts thereof.

68. **(Original)** The method of claim 67, wherein said anti-malarial compound is selected from the group consisting of: proguanil, chlorproguanil, trimethoprim, chloroquine, mefloquine, lumefantrine, atovaquone, pyrimethamine-sulfadoxine, pyrimethamine-dapsone, halofantrine, quinine, quinidine, amodiaquine, amopyroquine, sulphonamides, artemisinin, arteflene, artemether, artesunate, primaquine, pyronaridine, 1,16-hexadecamethylenebis(N-methylpyrrolidinium)dibromide, and combinations thereof.

69. **(Previously Presented)** A method for preventing malaria in a mammal, comprising administering to said mammal an effective amount of a substituted tetracycline compound, such that malaria is prevented in said mammal, wherein said tetracycline compound is of formula I:



wherein:

X is CR^{6'}R⁶;

R², R^{2'}, R^{4'}, and R^{4''} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ is NR^{4'}R^{4''}, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R³, R¹¹ and R¹² are each hydrogen, or a pro-drug moiety;

R¹⁰ is hydrogen, or a prodrug moiety;

R⁵ is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

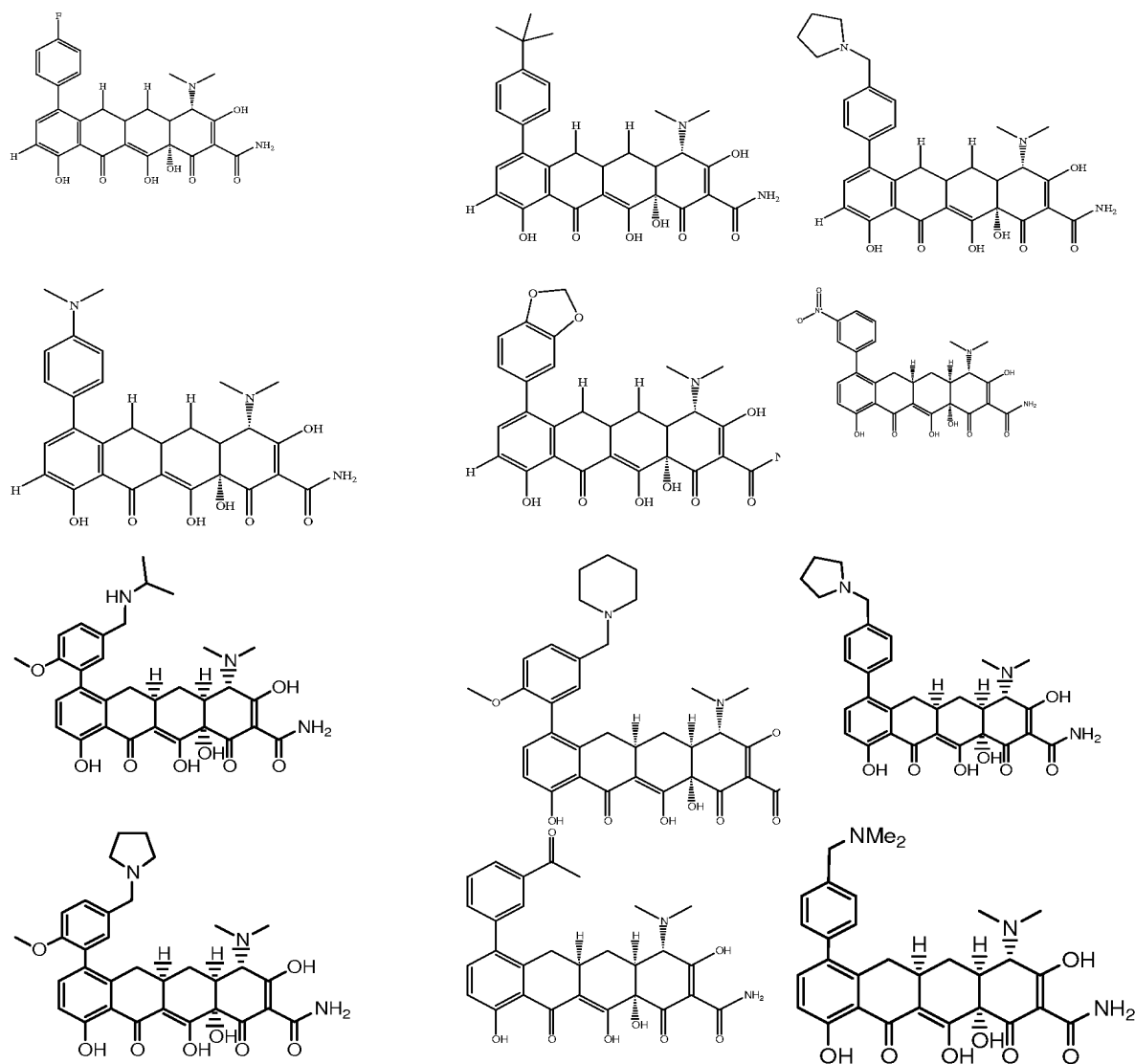
R⁶ and R^{6'} are independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

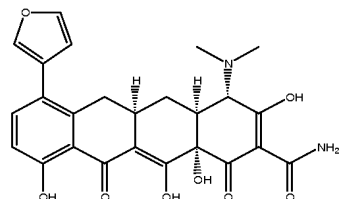
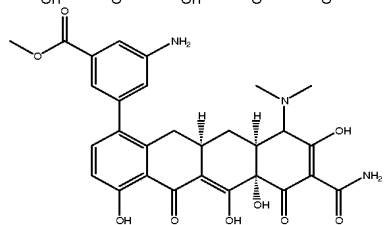
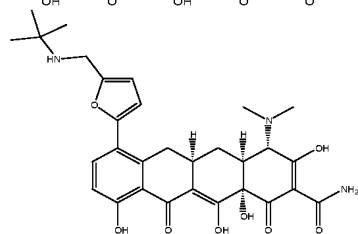
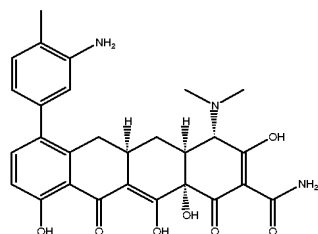
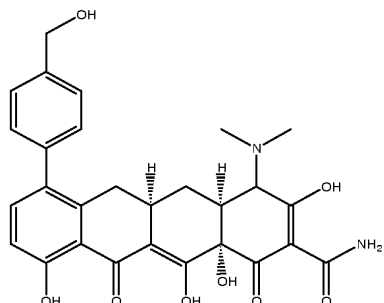
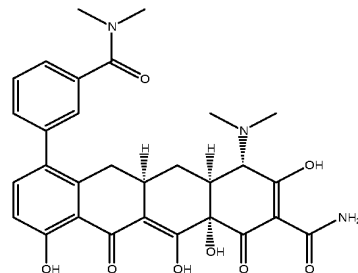
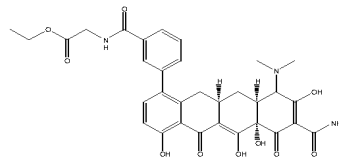
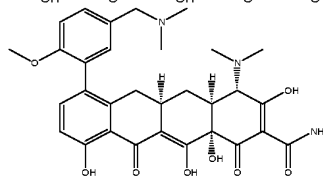
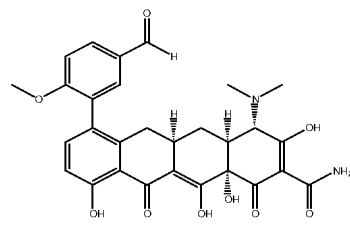
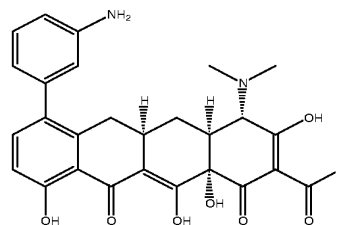
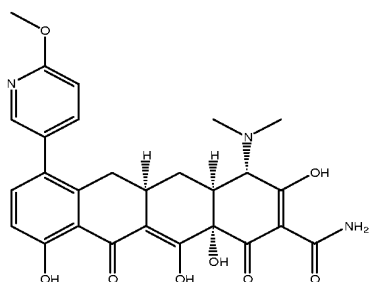
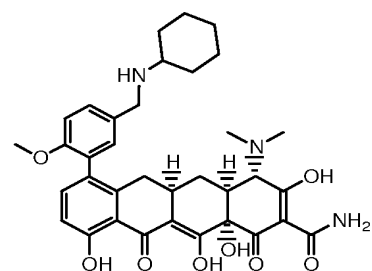
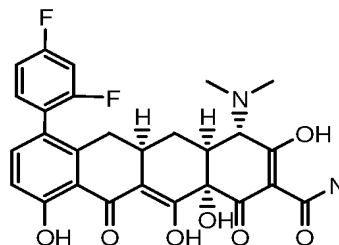
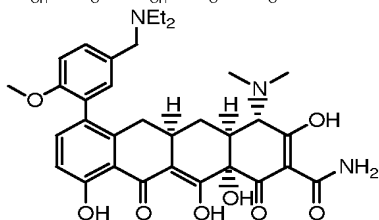
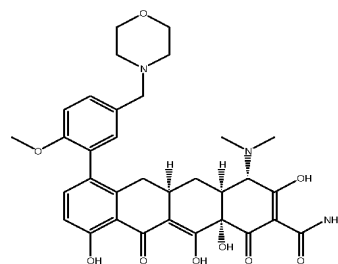
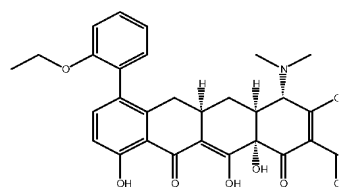
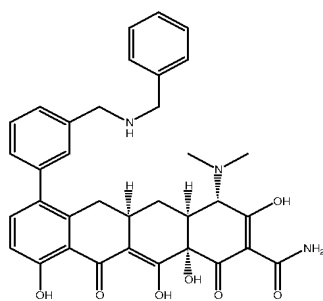
R^7 is aryl;

R^9 is hydrogen;

R^8 is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and pharmaceutically acceptable salts thereof.

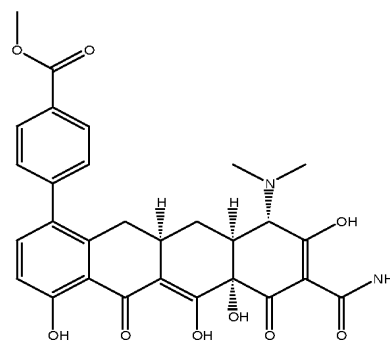
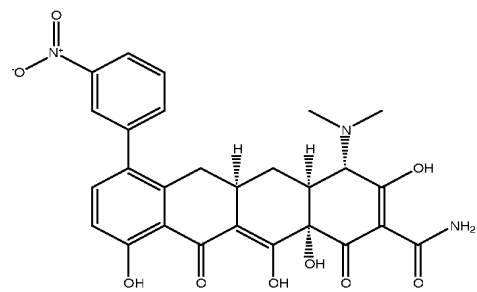
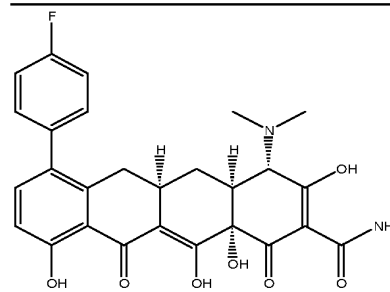
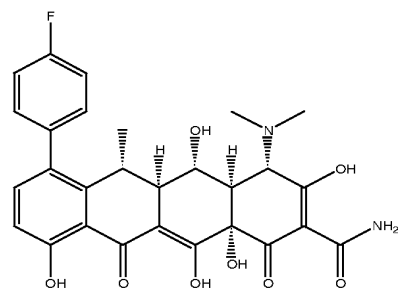
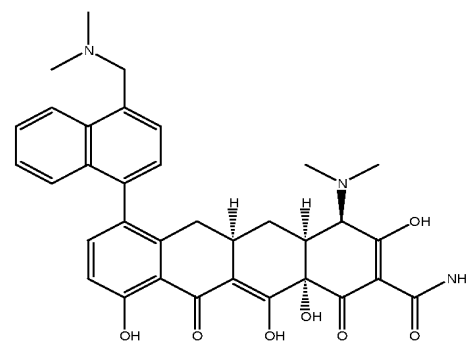
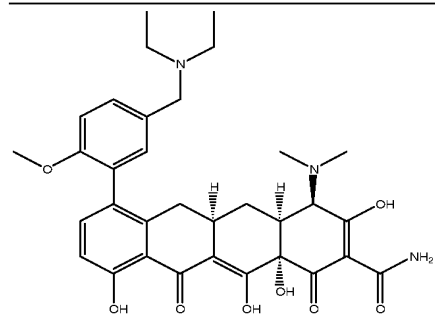
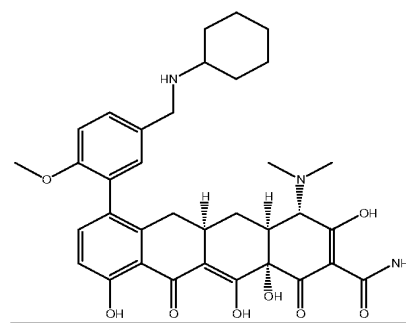
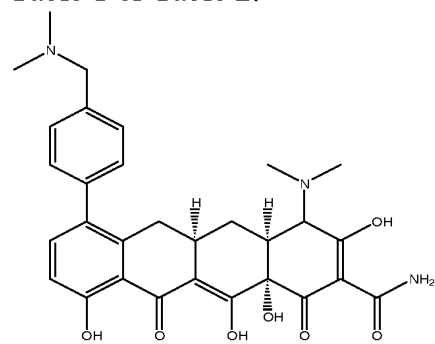
70. **(Currently Amended)** The method of claim 69, wherein said substituted tetracycline compound is selected from the group consisting of:

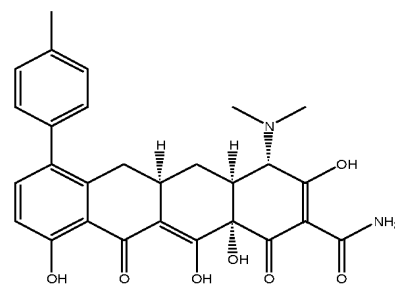
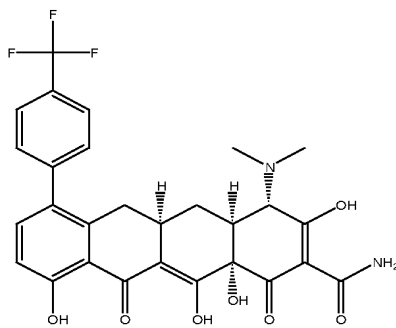
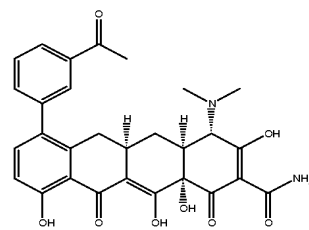
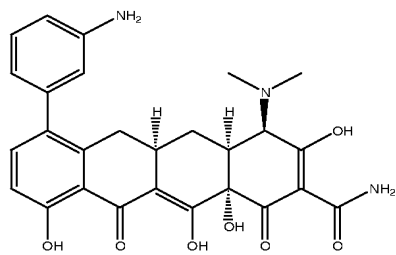
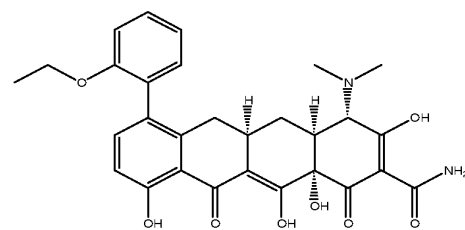
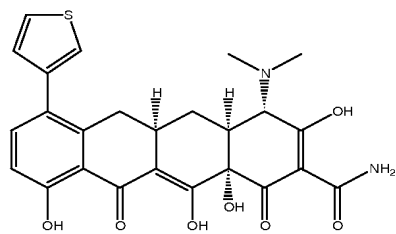
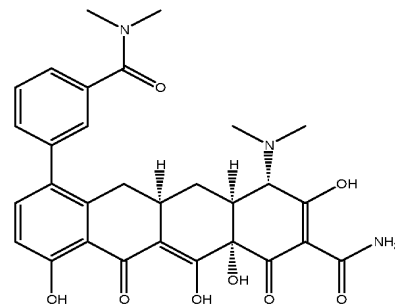
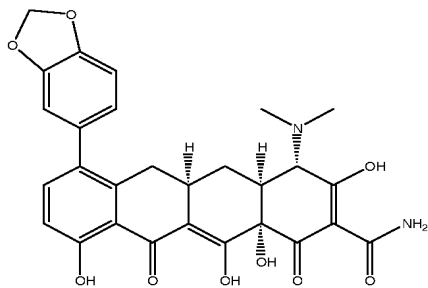
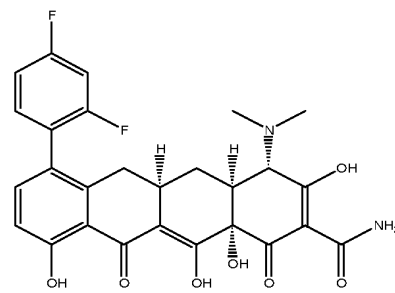
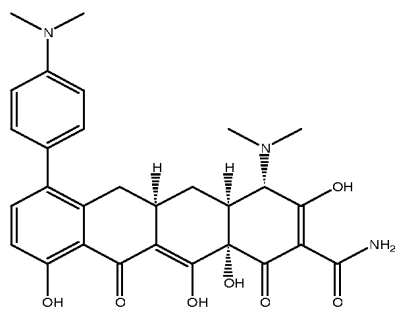


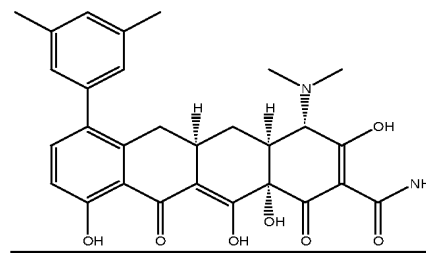
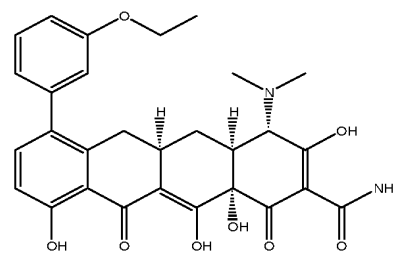
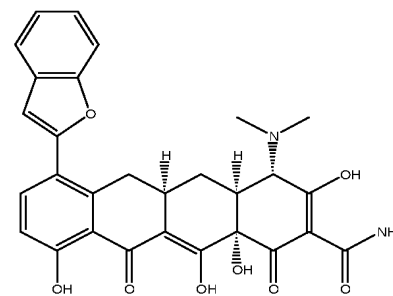
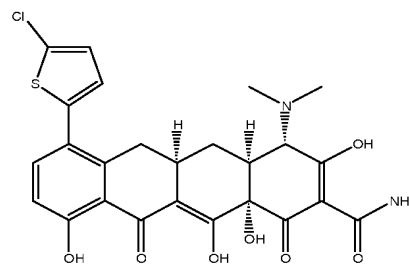
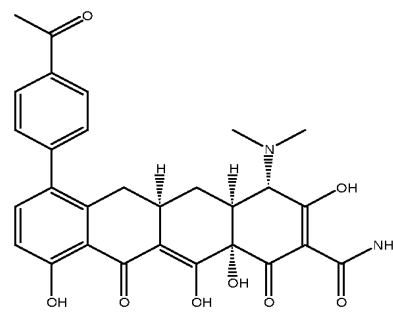
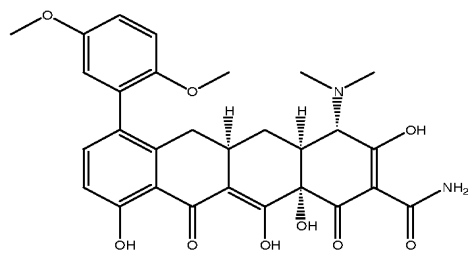
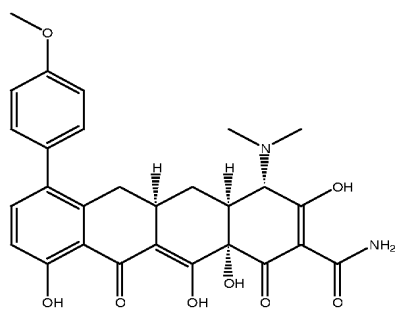
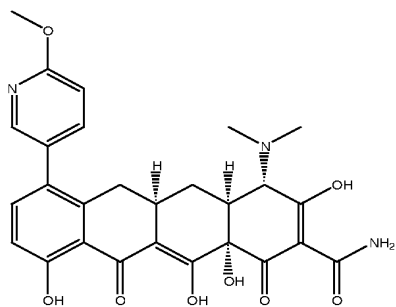
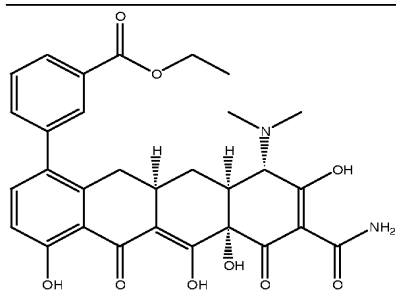
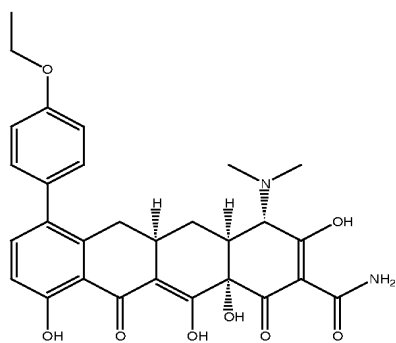


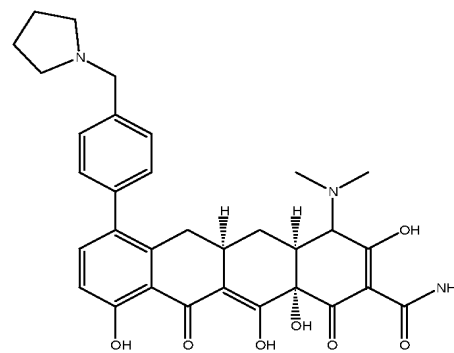
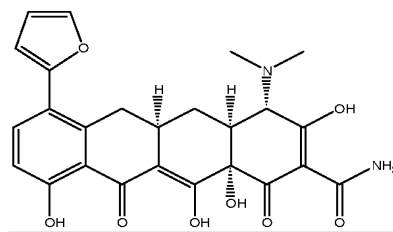
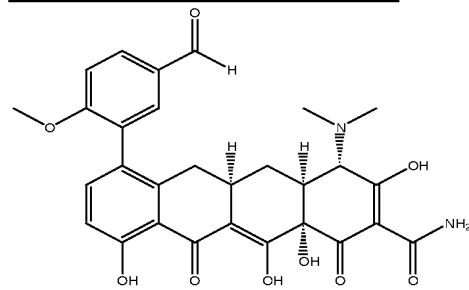
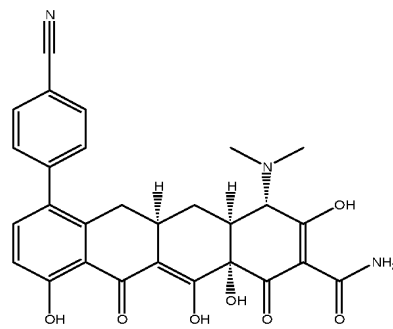
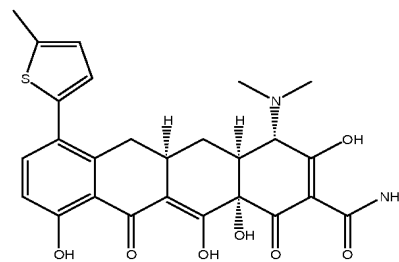
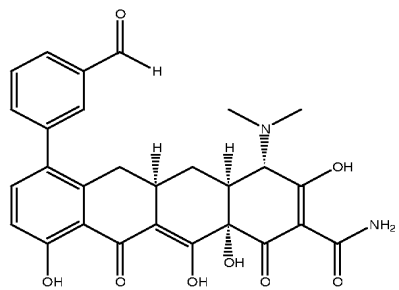
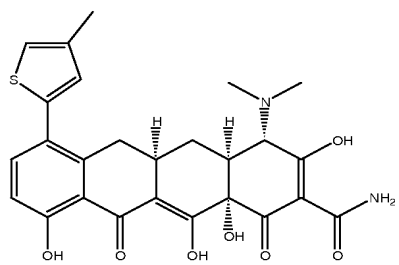
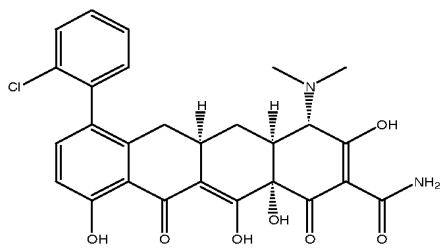
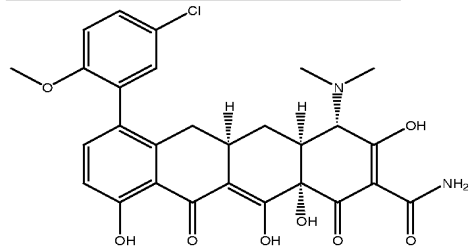
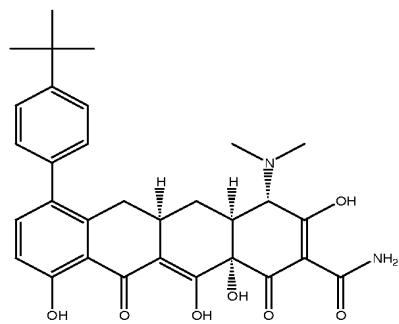
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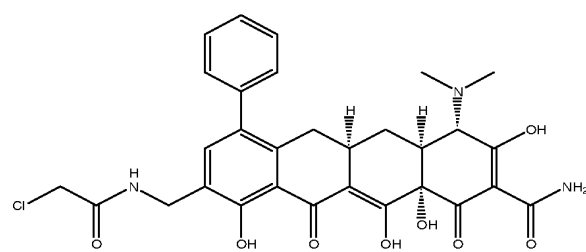
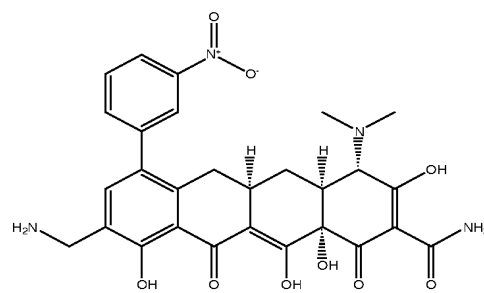
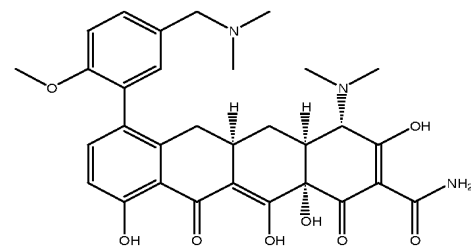
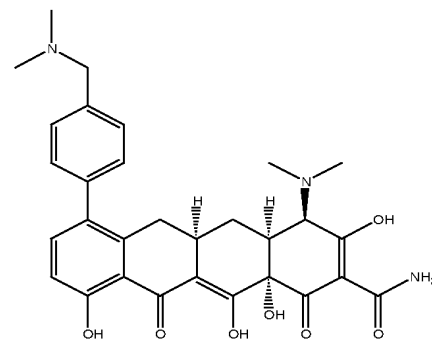
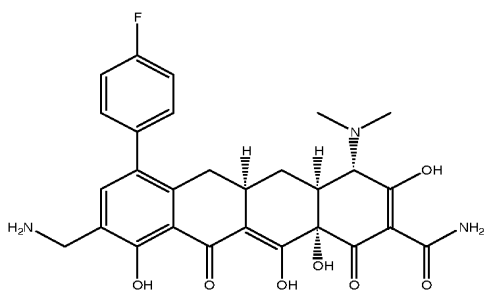
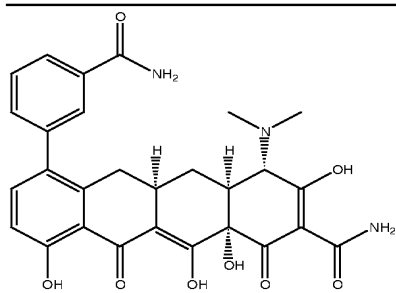
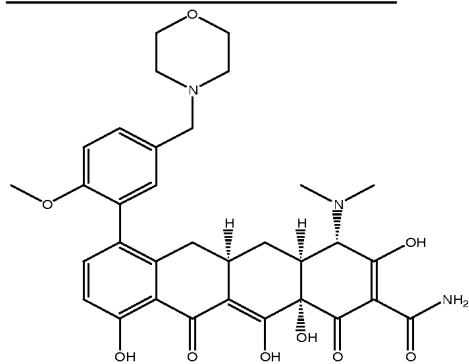
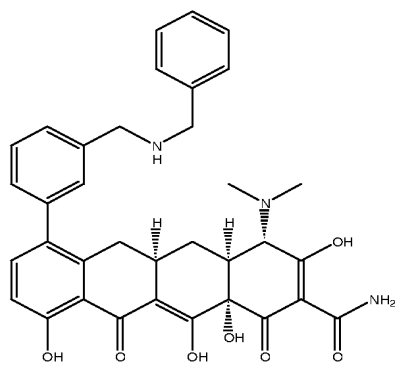
71. **(Currently Amended)** The method of claim 67 or 69, wherein said substituted tetracycline compound is selected from the group consisting of: a compound shown in Table 1 or Table 2.

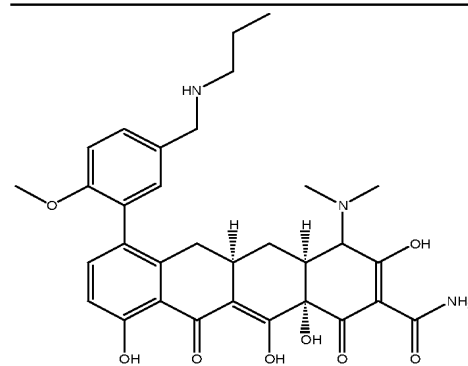
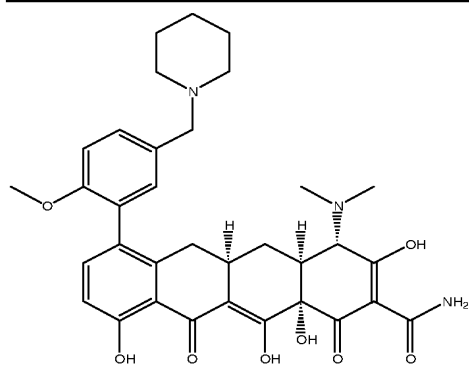
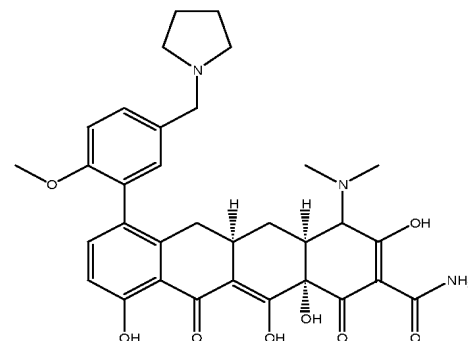
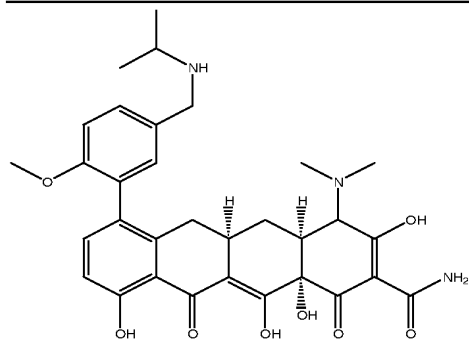
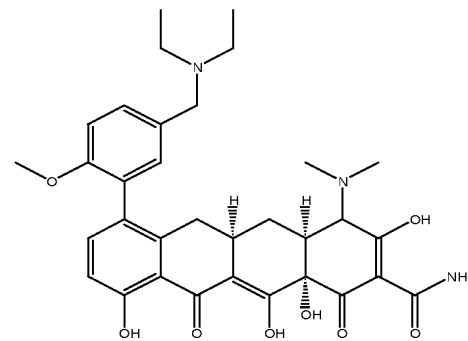
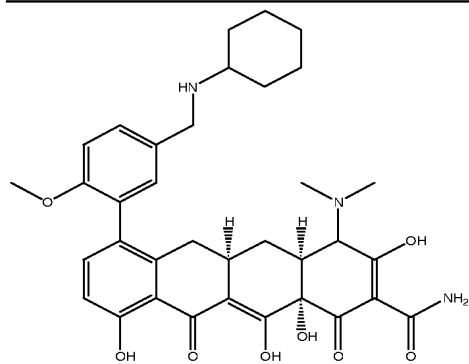
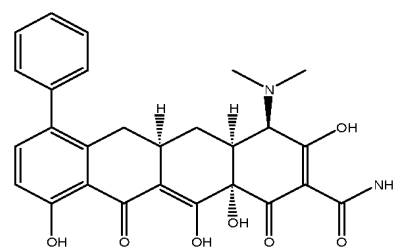
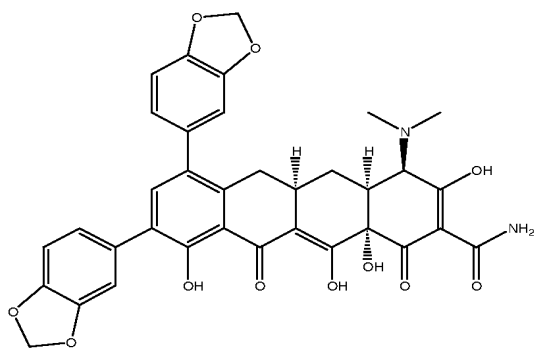


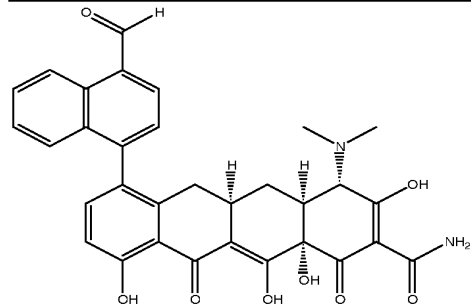
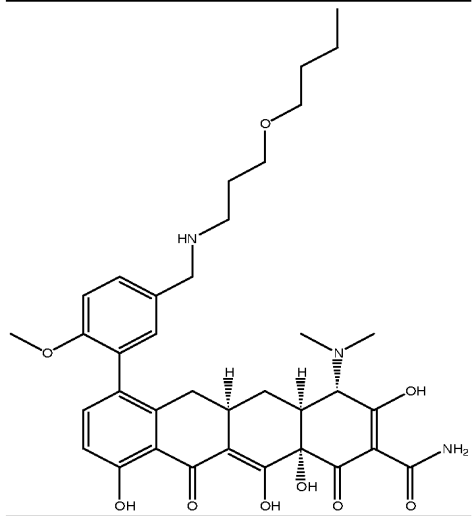
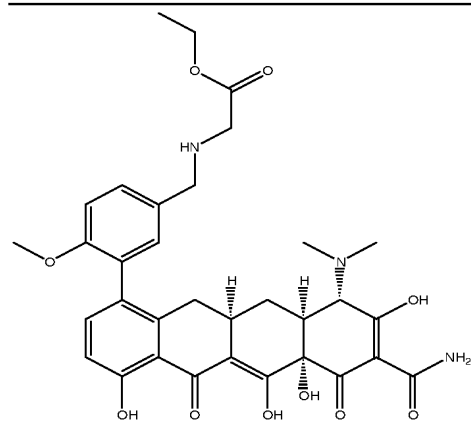
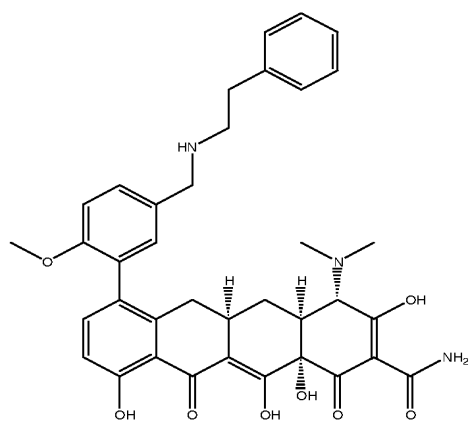
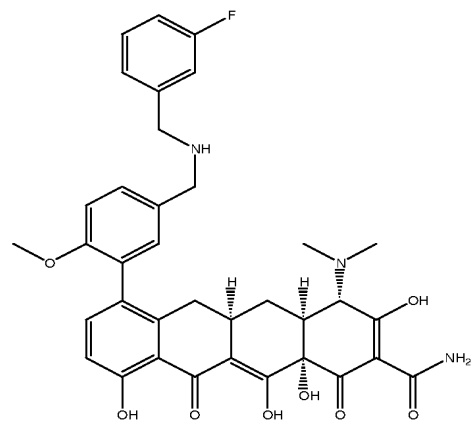
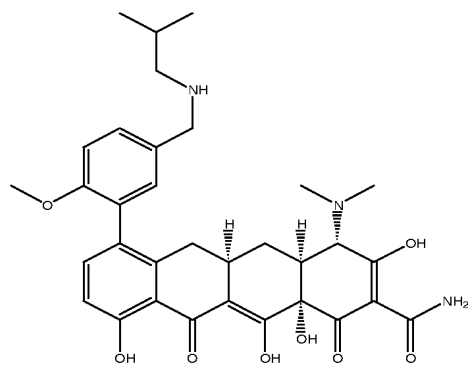


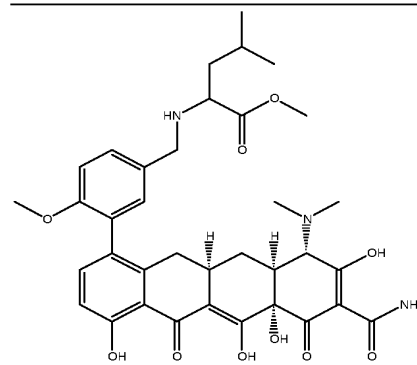
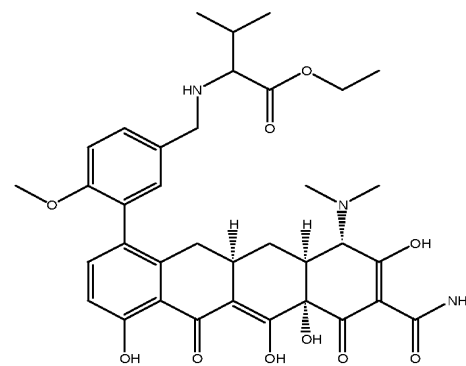
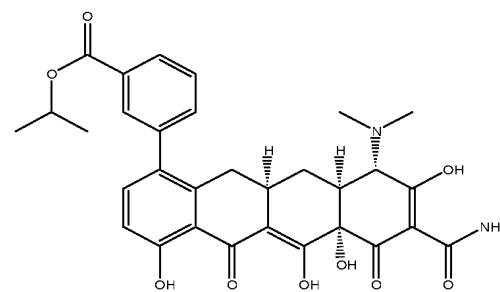
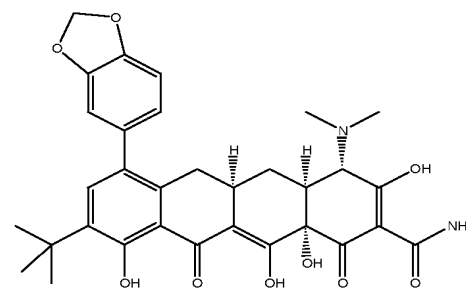
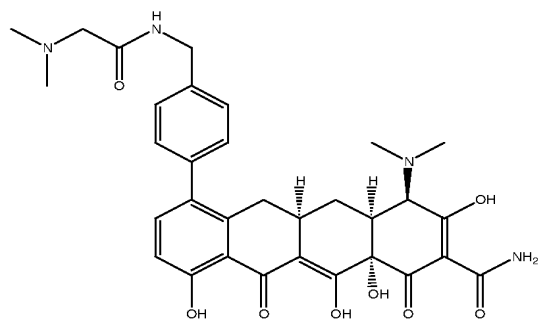
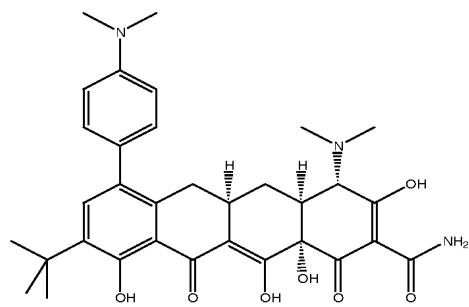
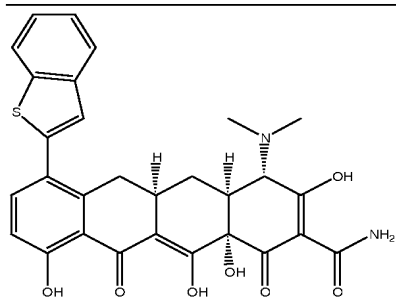
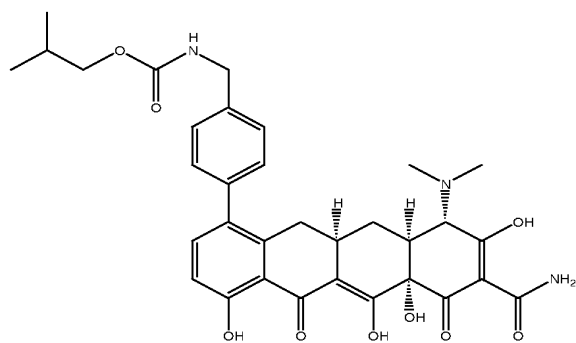


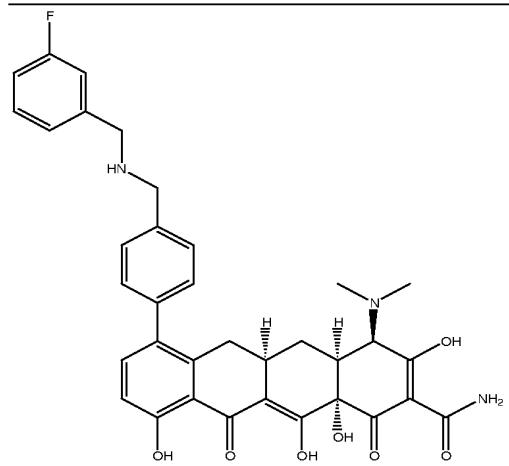
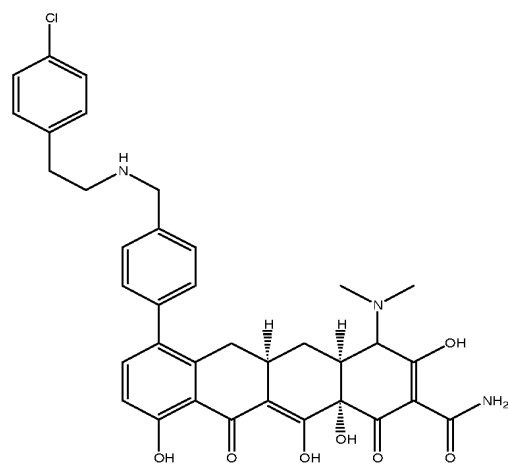
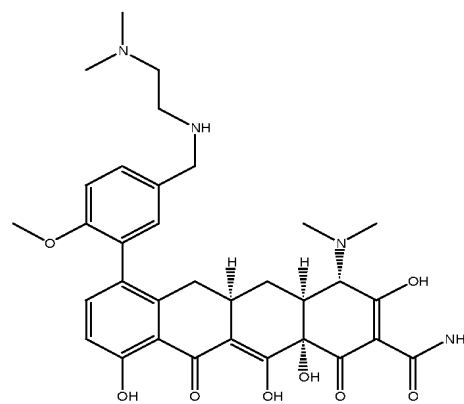
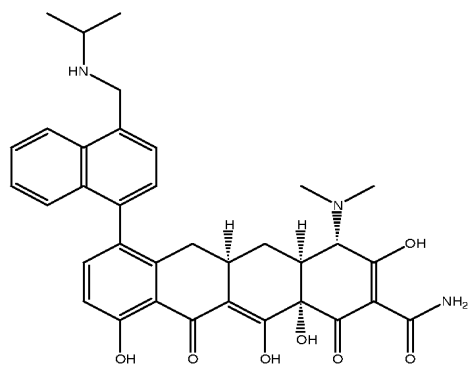
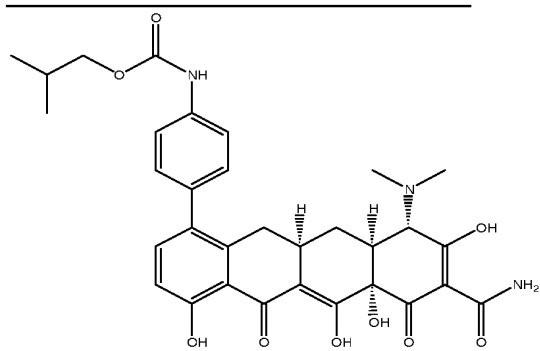
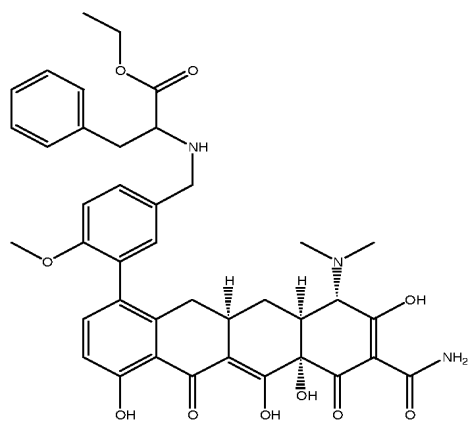


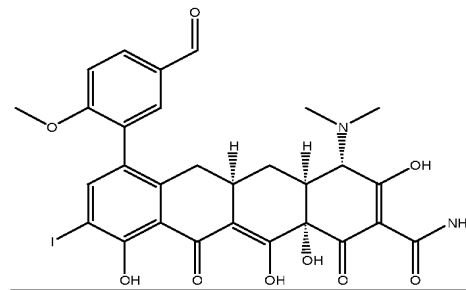
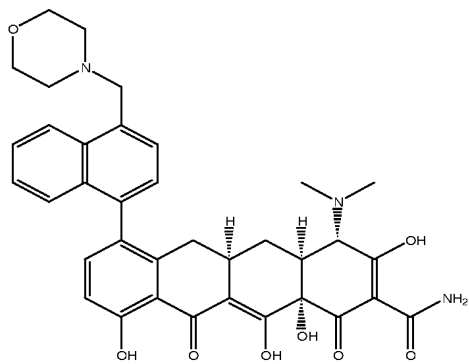
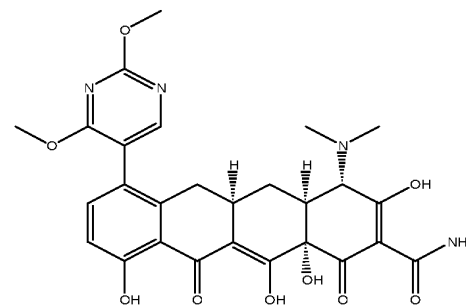
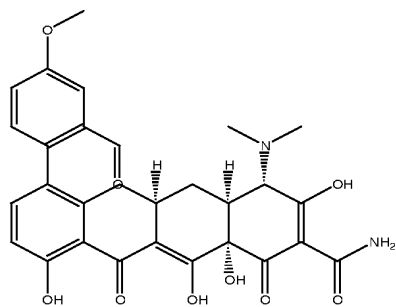
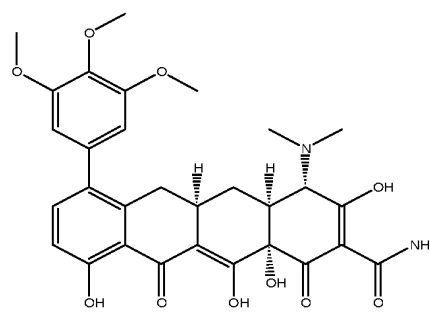
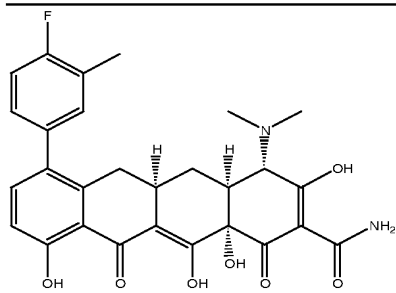
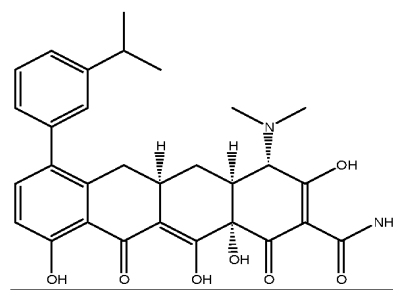
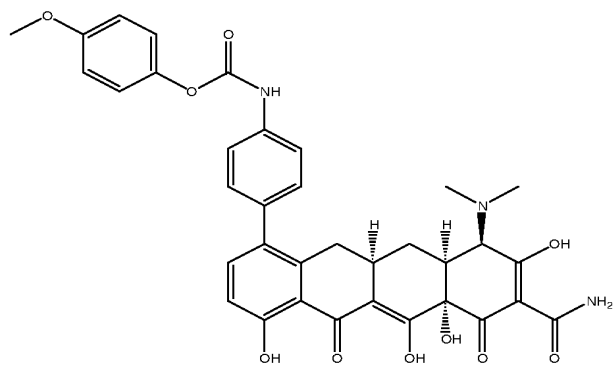


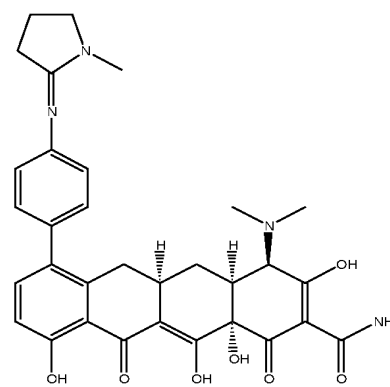
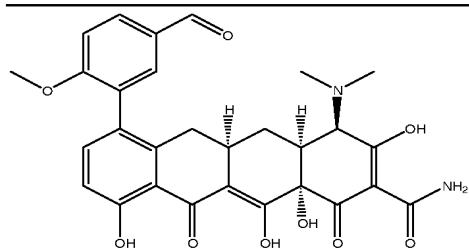
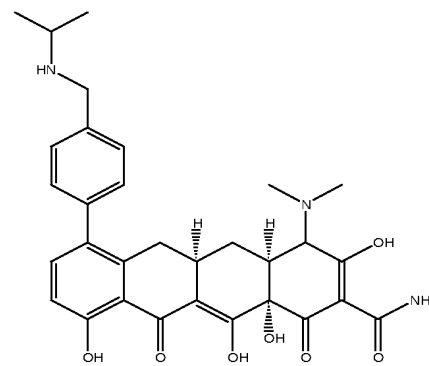
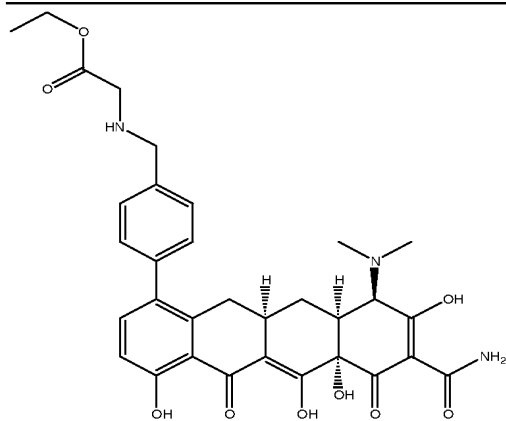
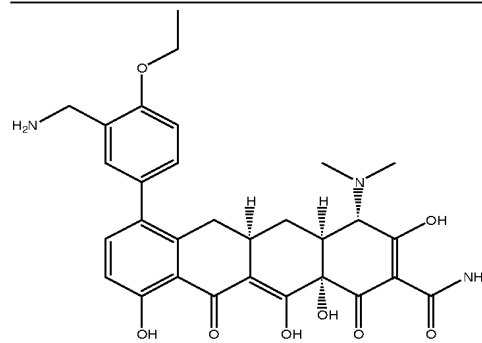
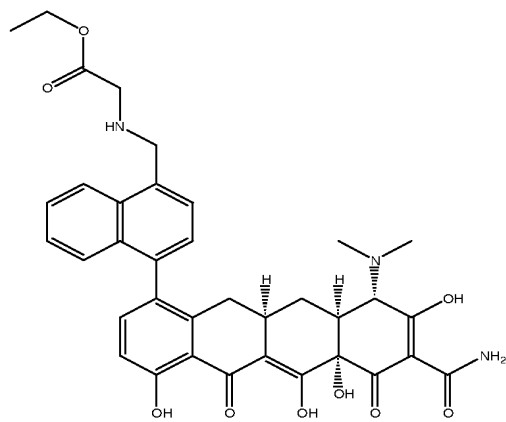
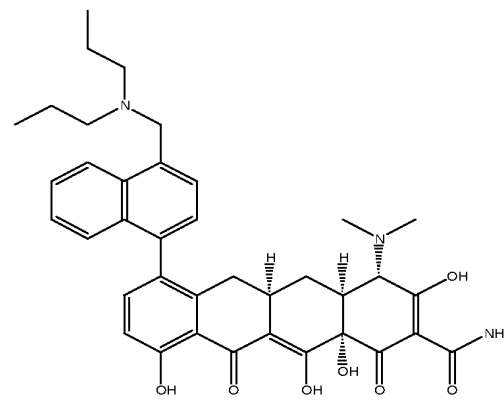
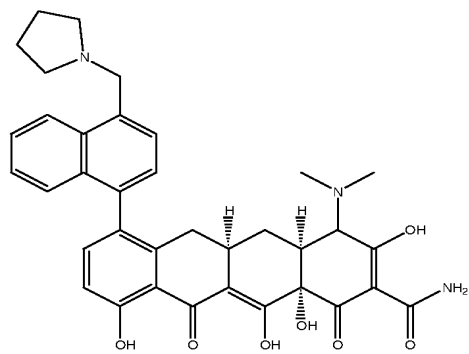


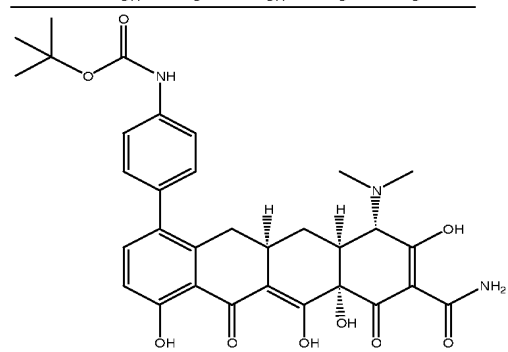
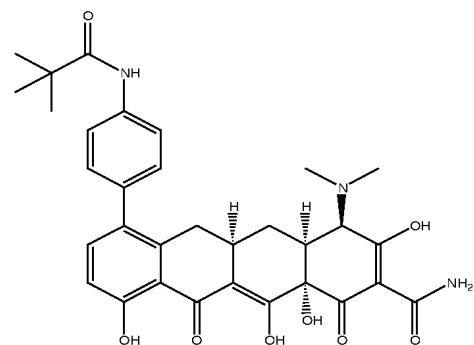
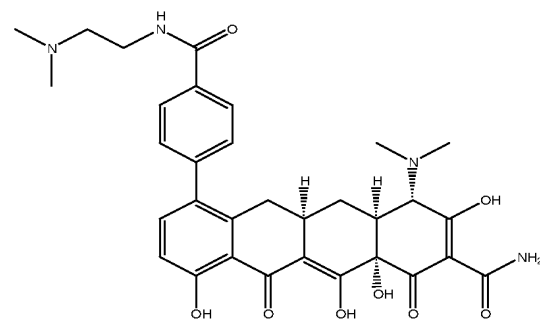
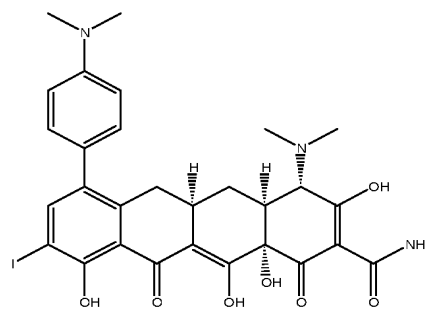
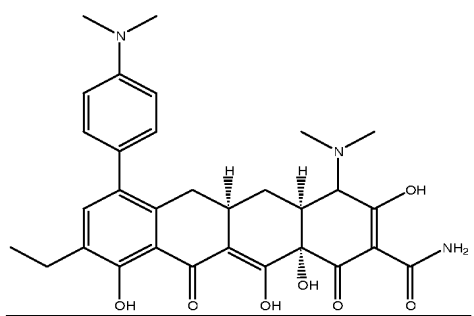
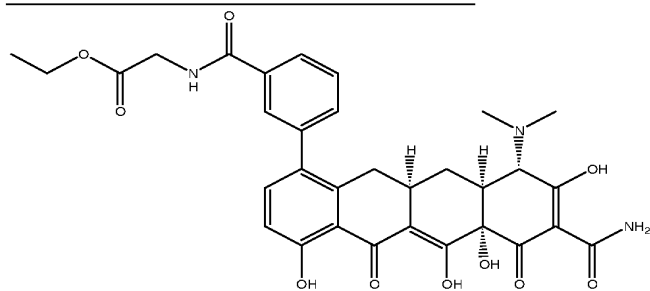
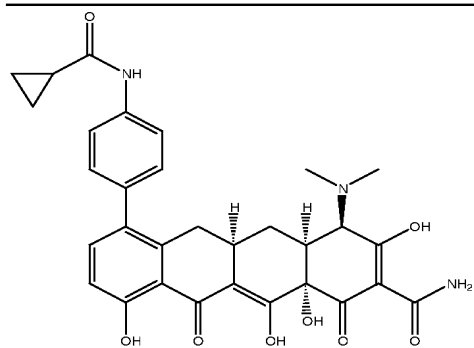
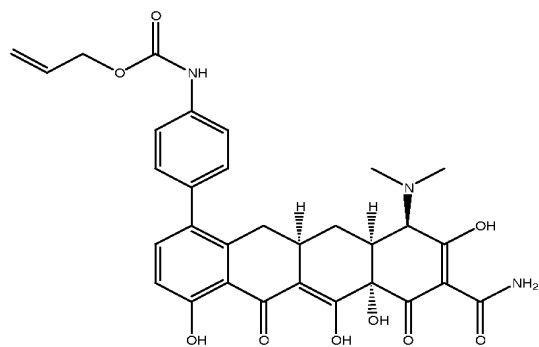


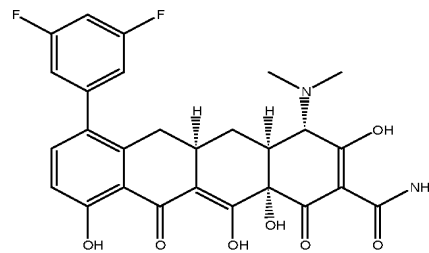
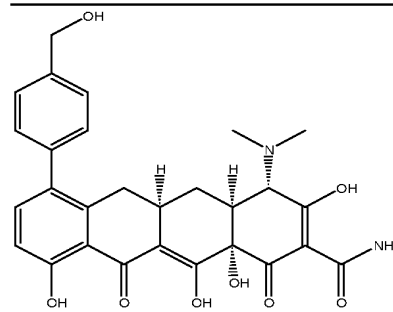
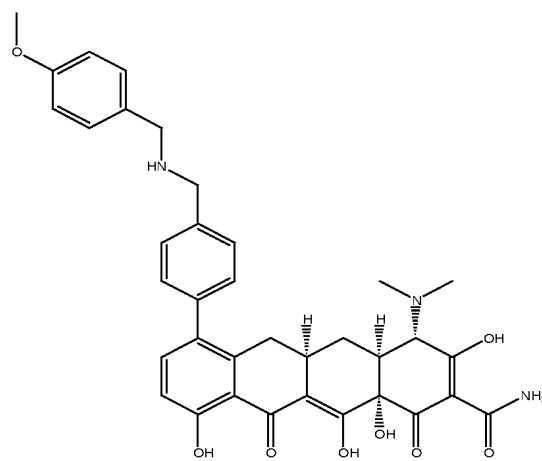
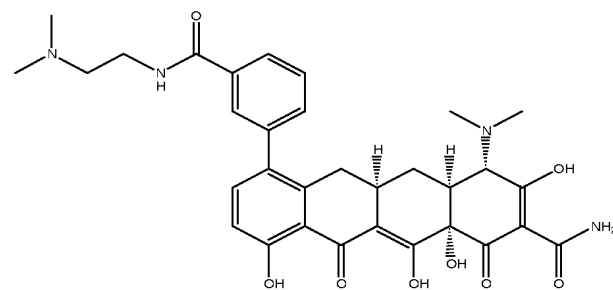
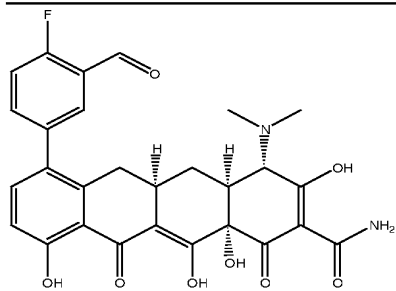
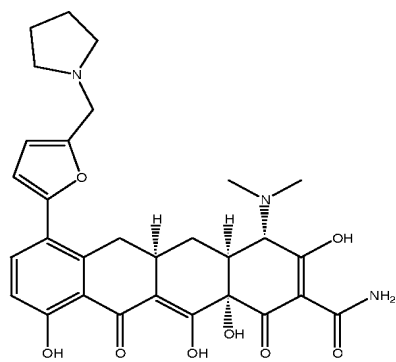
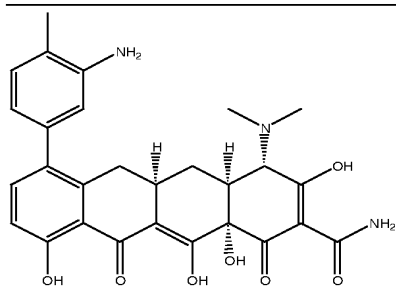
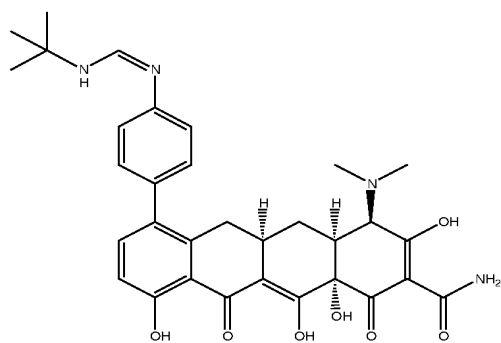


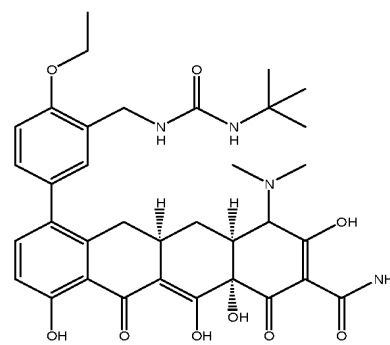
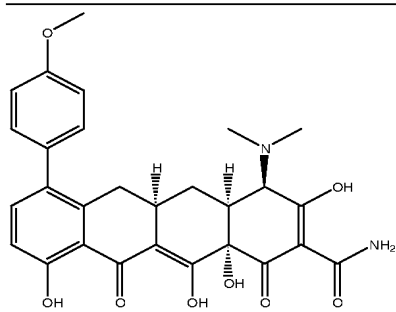
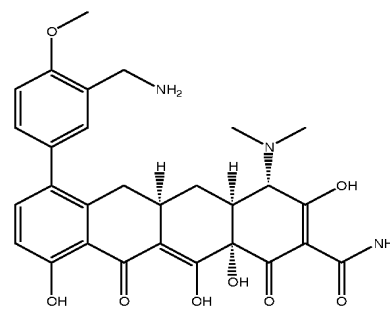
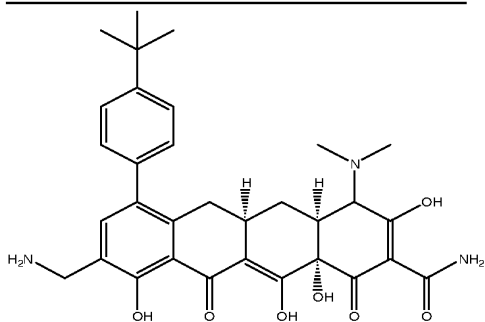
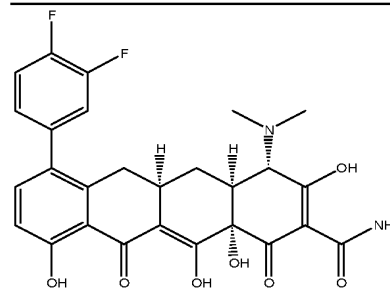
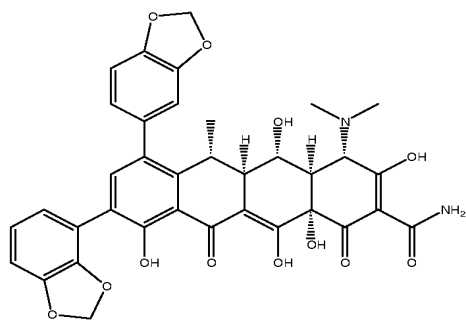
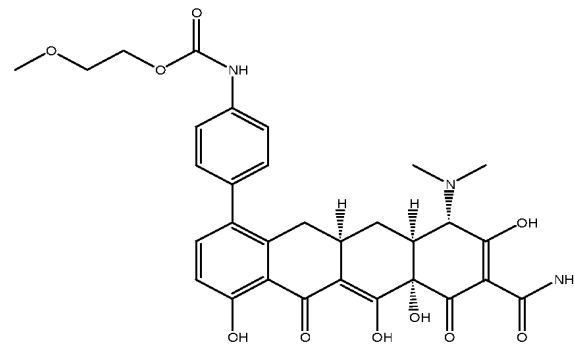
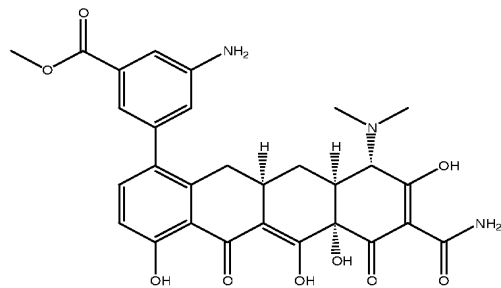
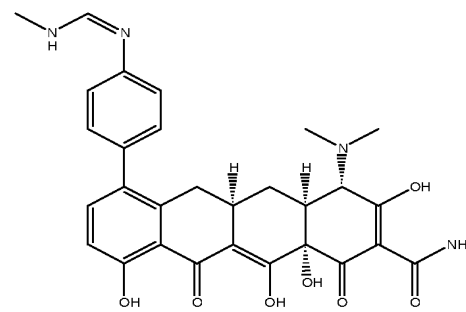
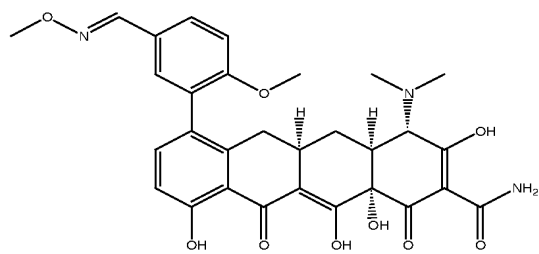


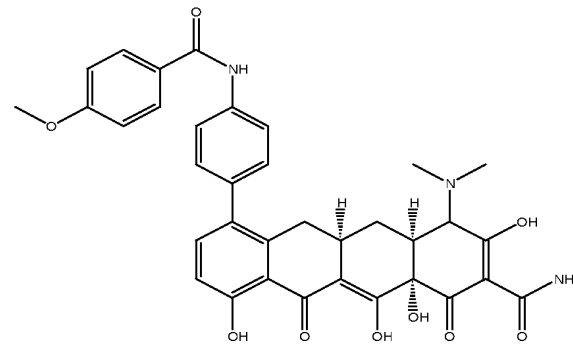
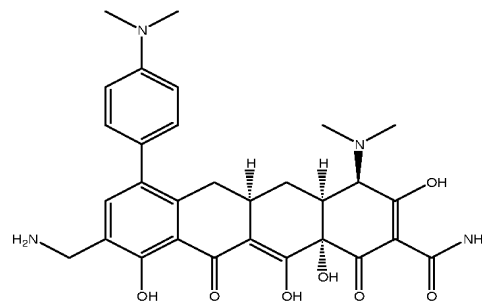
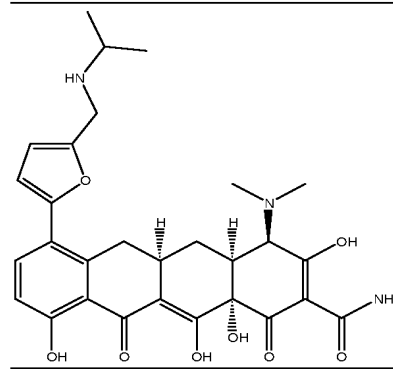
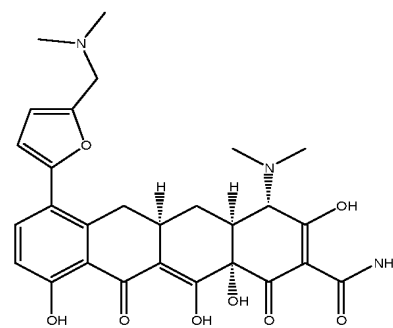
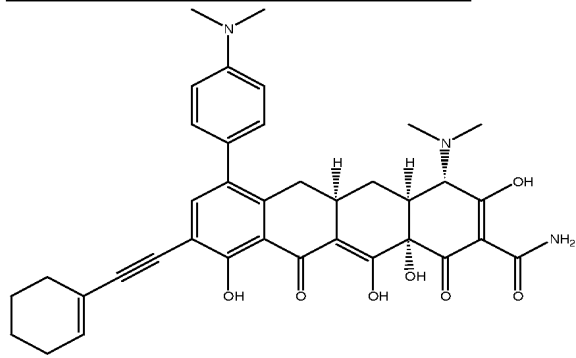
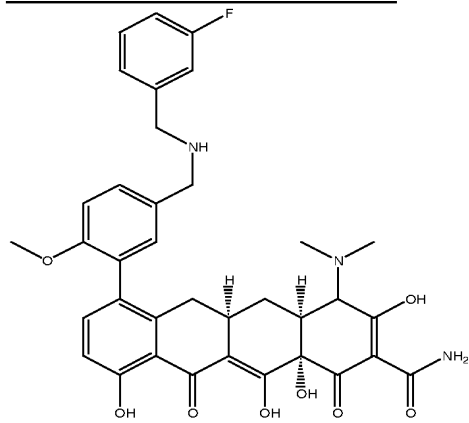
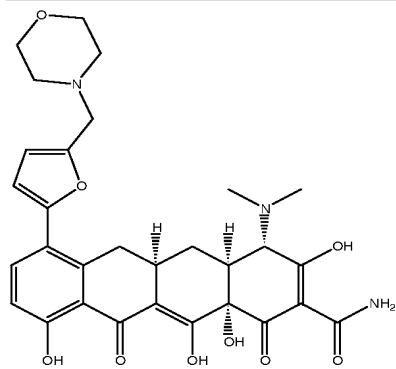
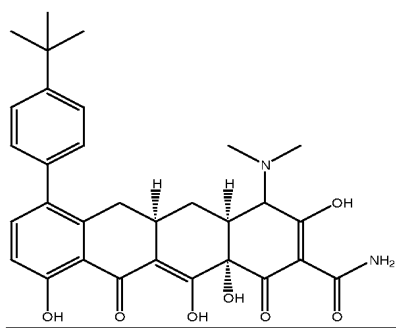


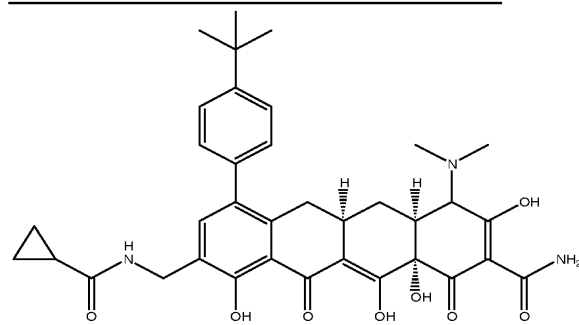
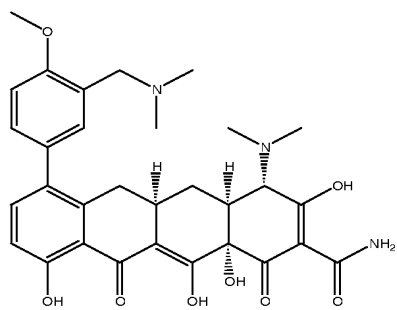
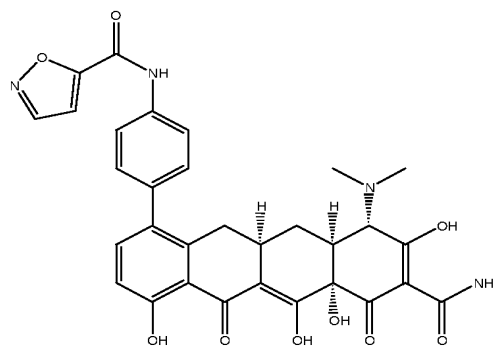
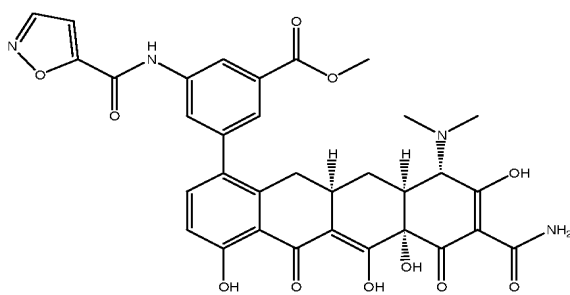
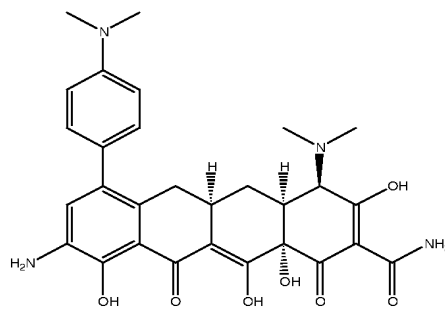
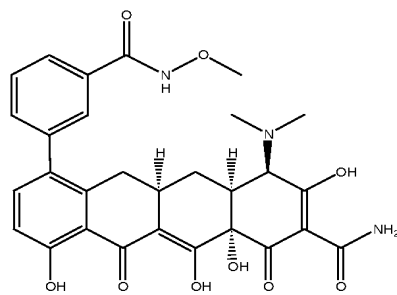
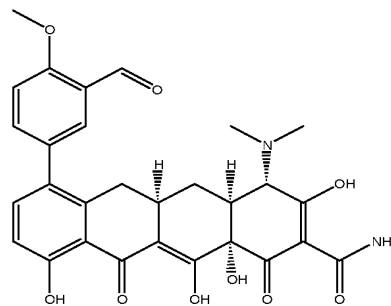
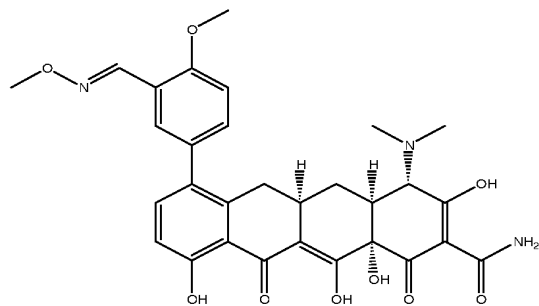
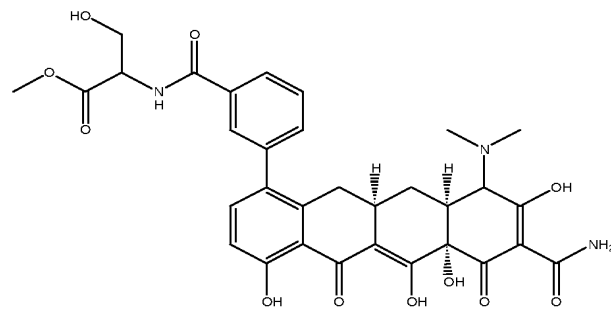
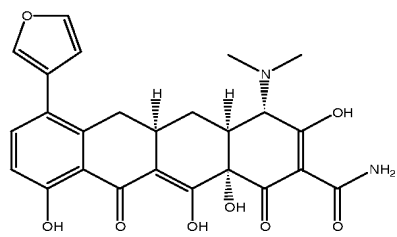


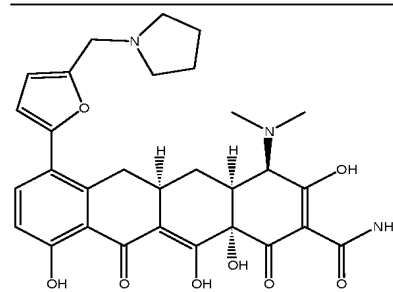
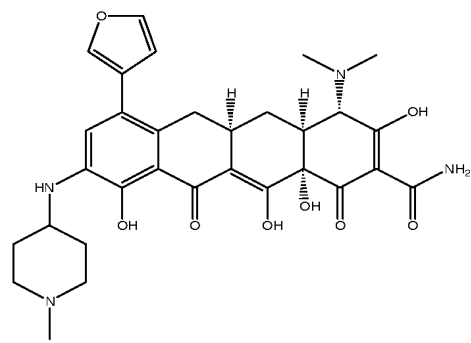
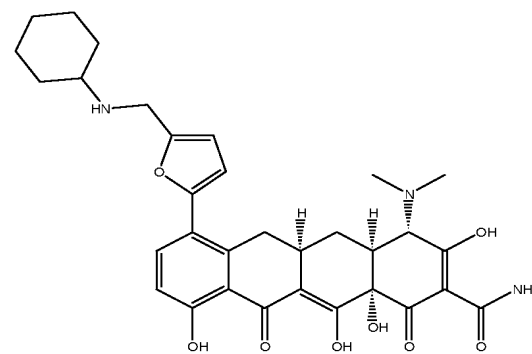
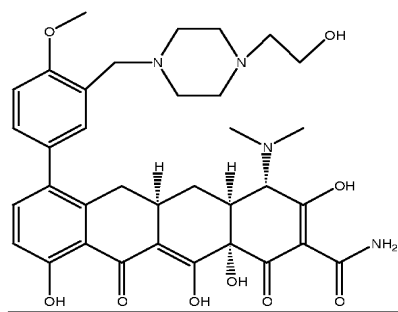
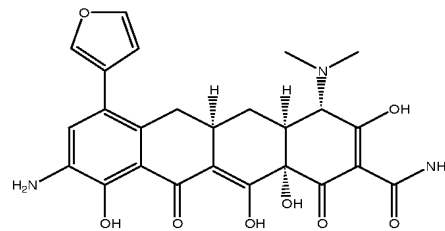
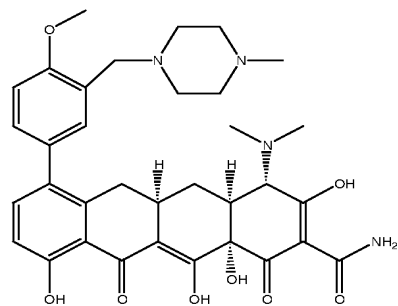
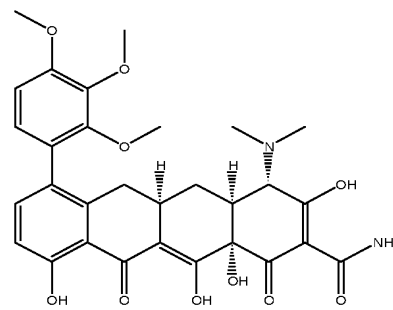
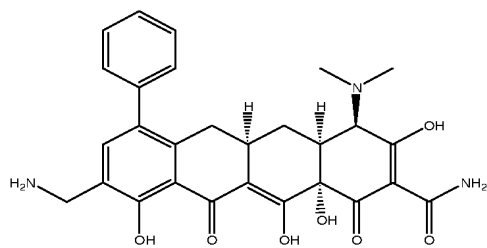


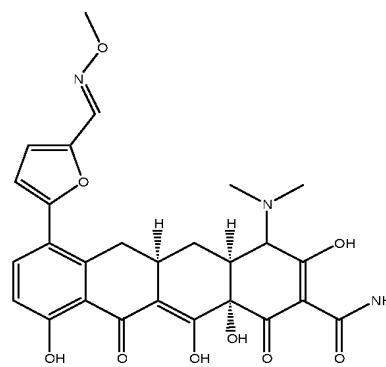
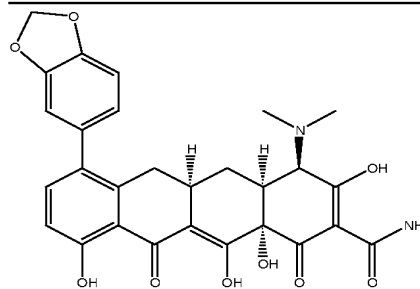
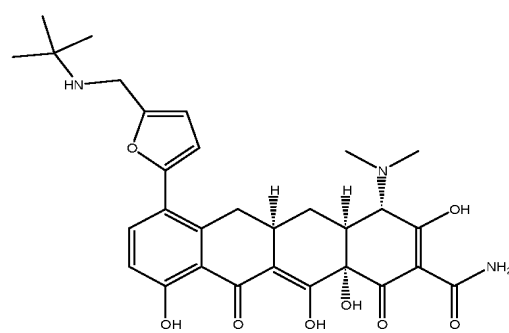
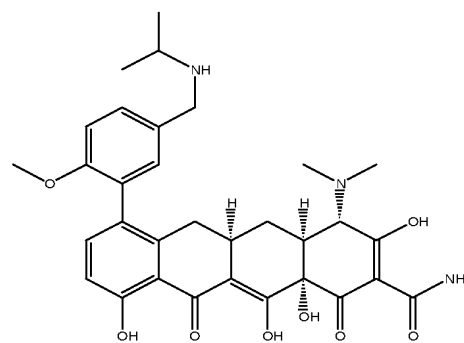
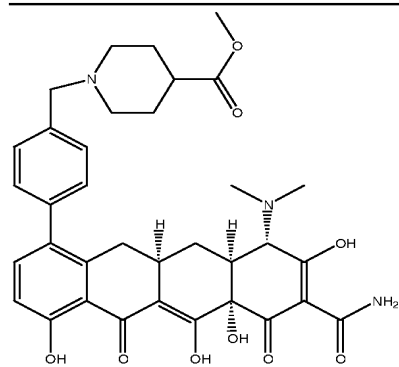
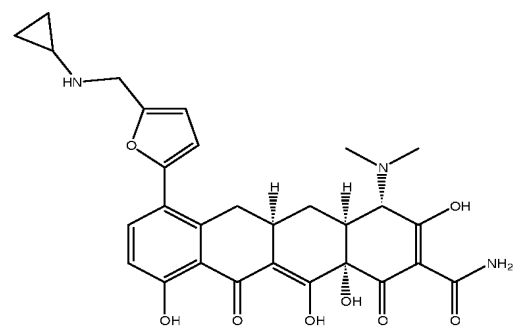
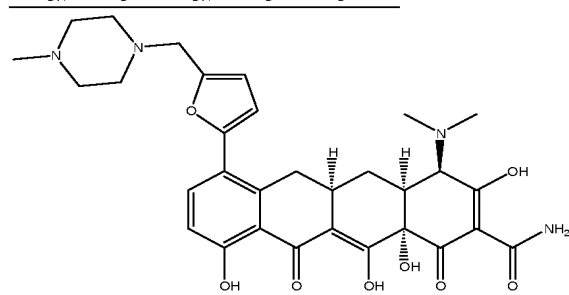
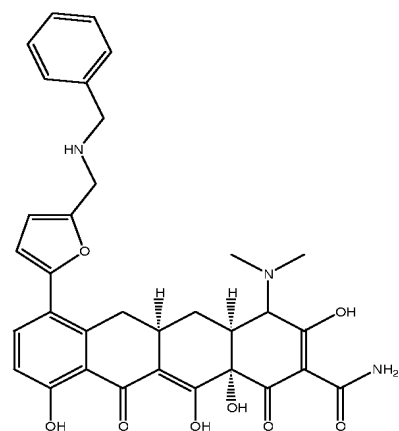


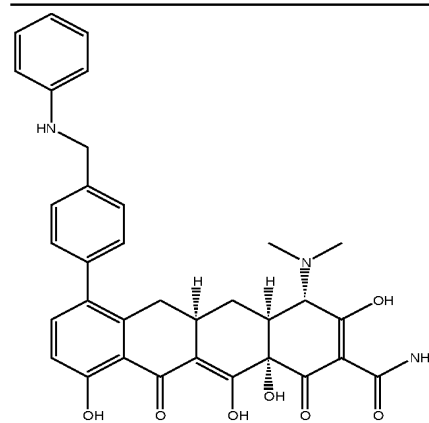
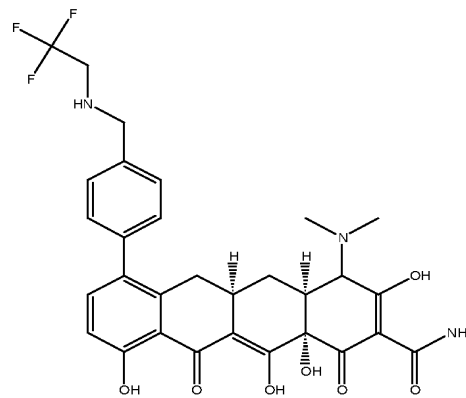
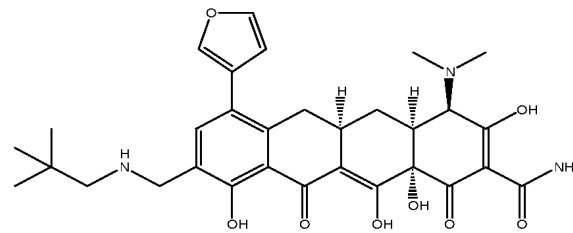
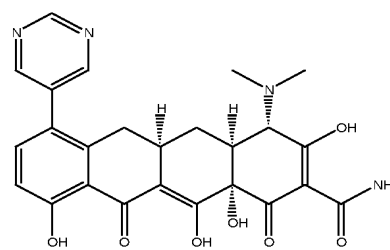
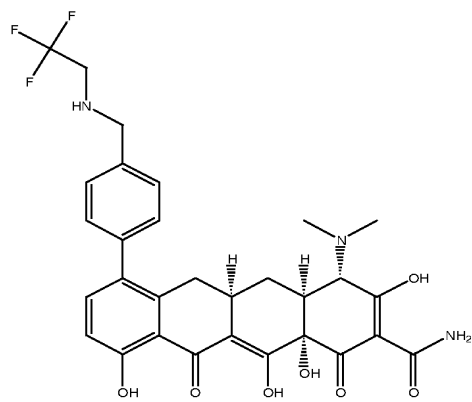
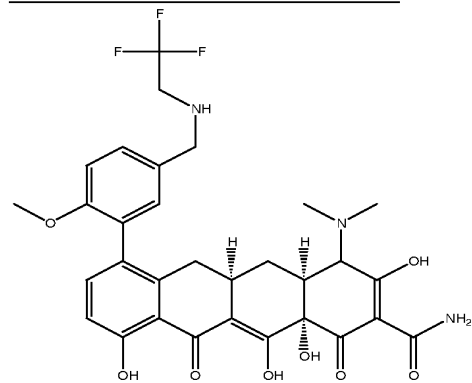
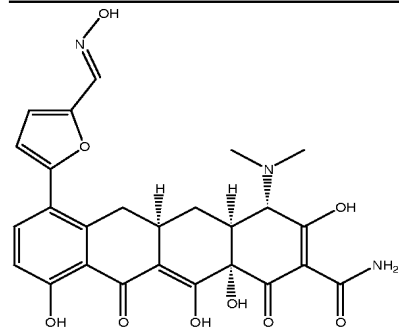
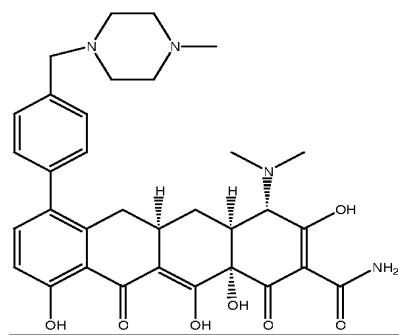


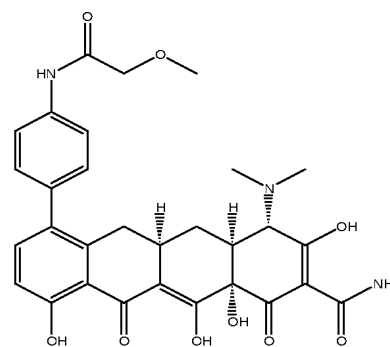
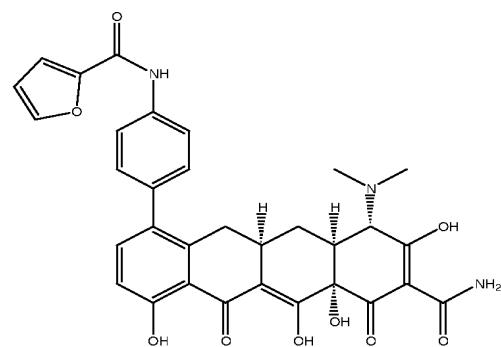
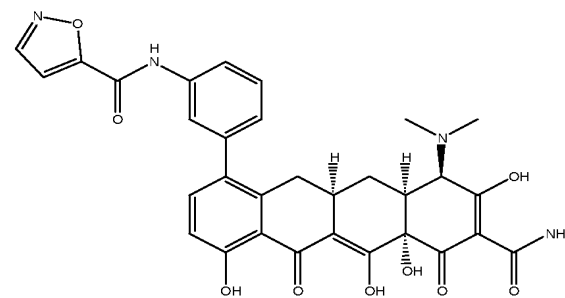
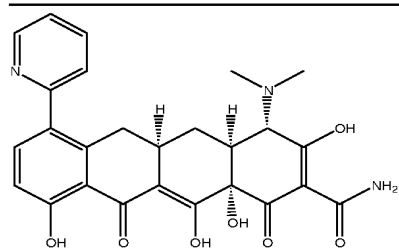
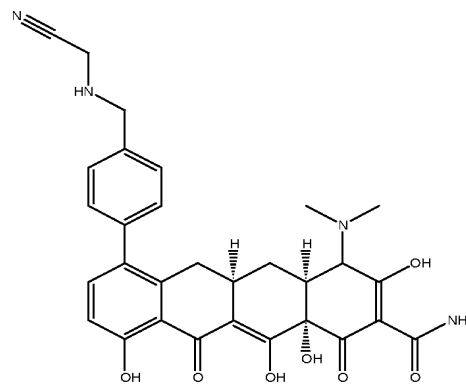
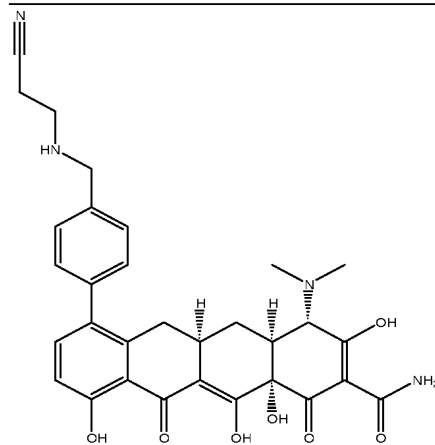
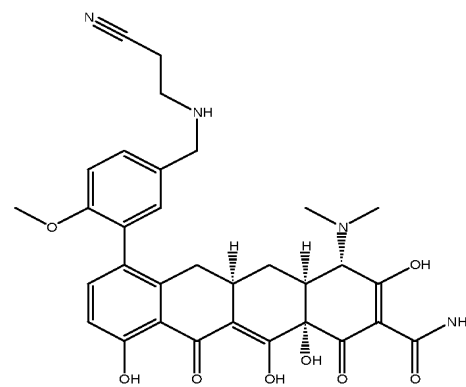
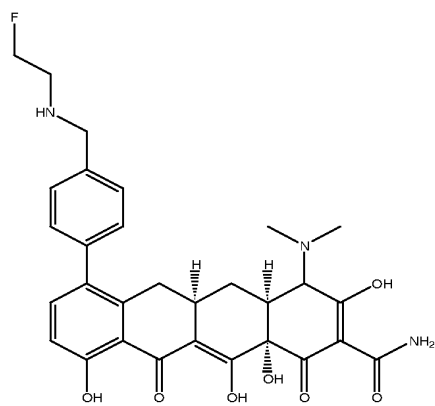


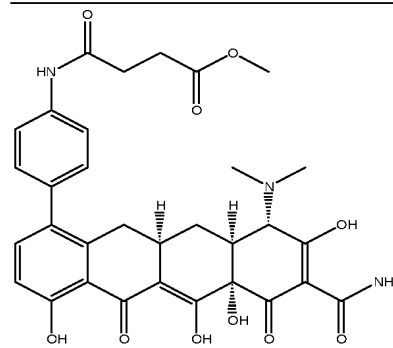
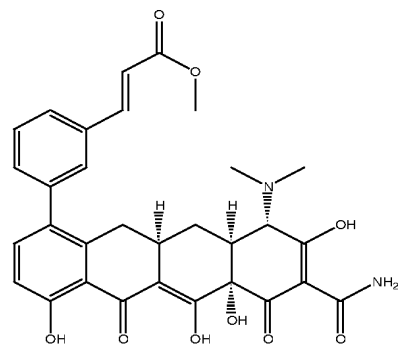
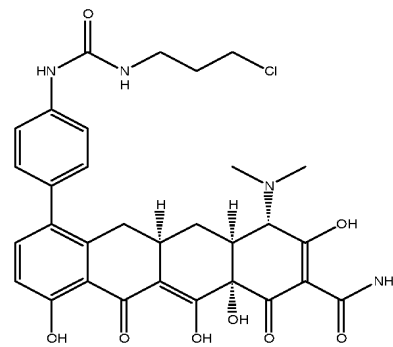
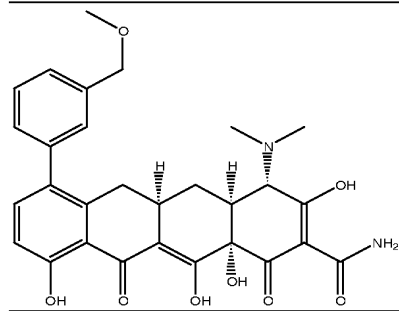
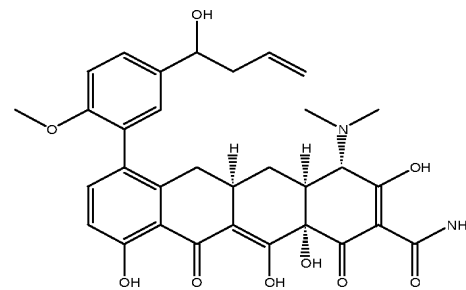
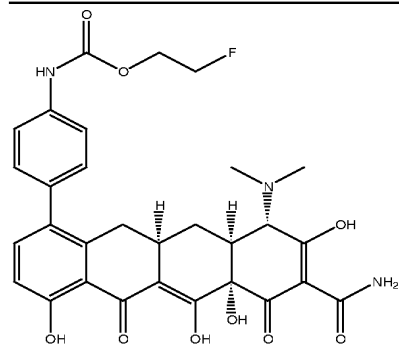
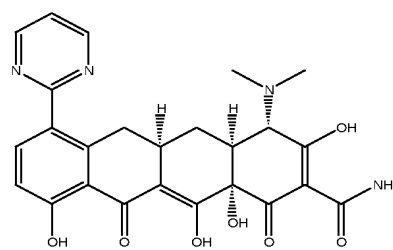
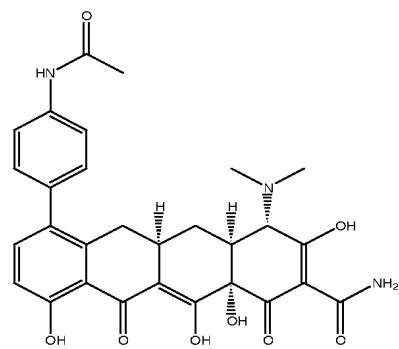


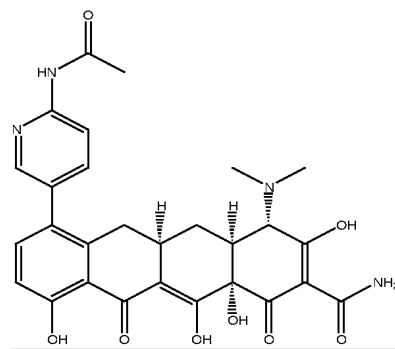
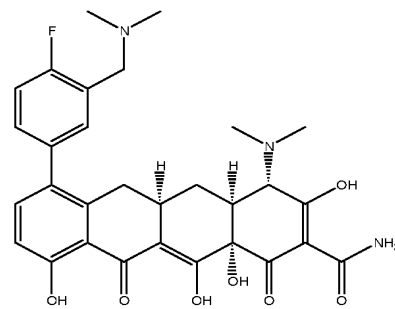
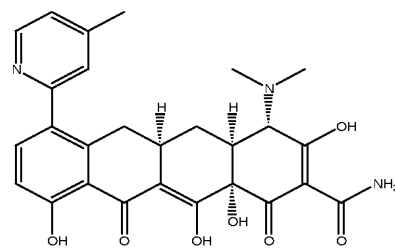
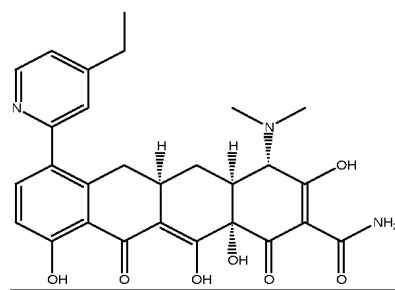
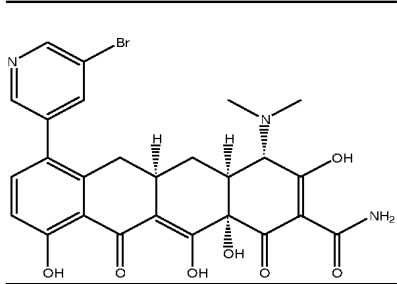
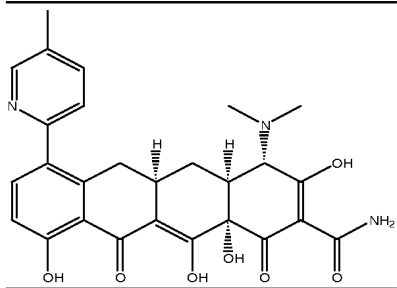
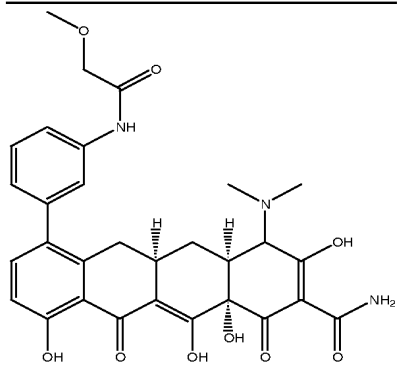
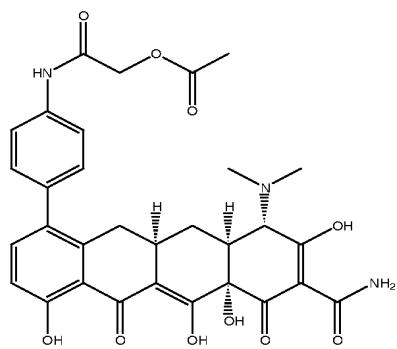


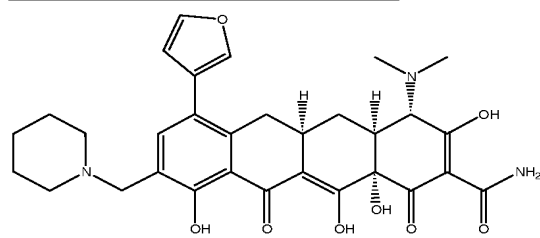
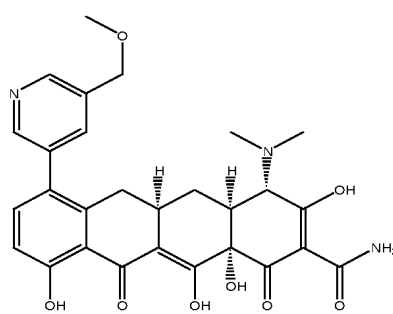
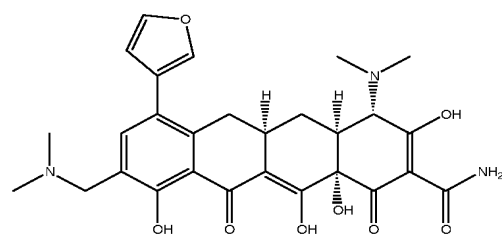
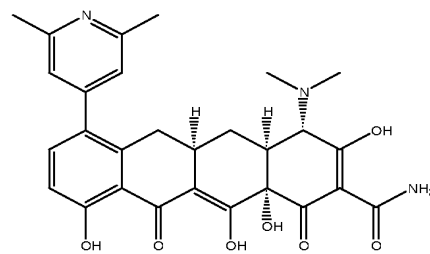


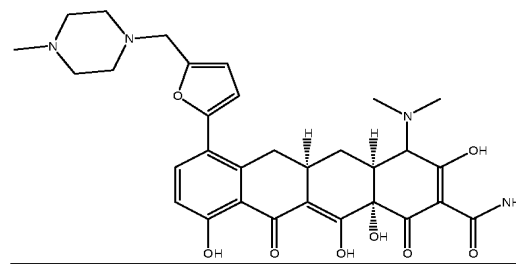
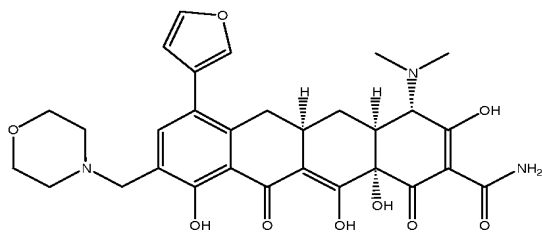
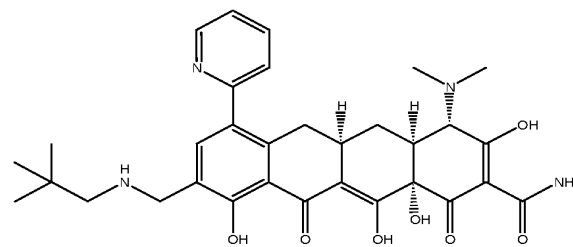
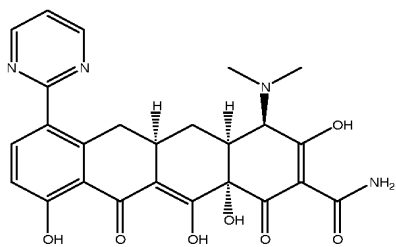
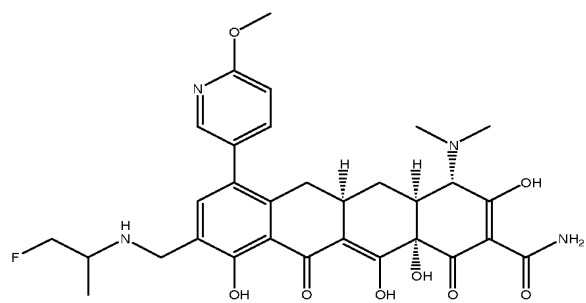
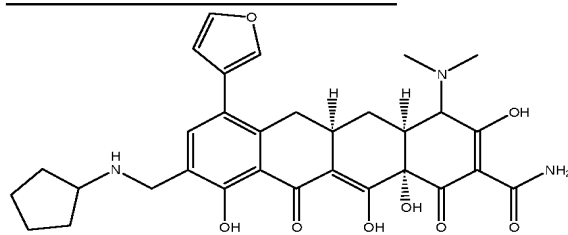
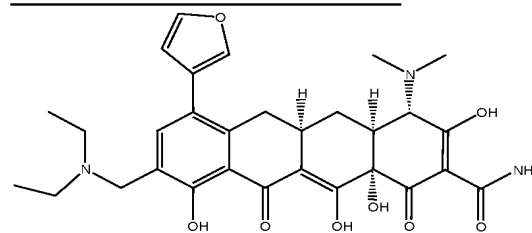
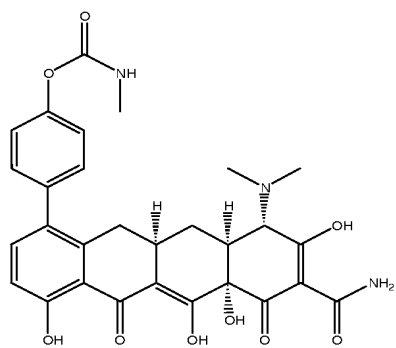
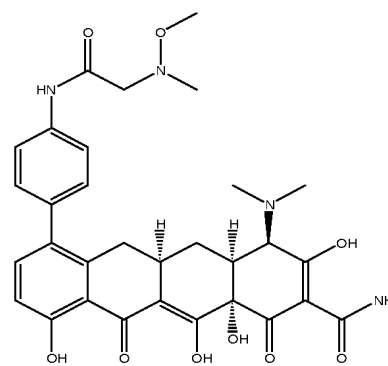
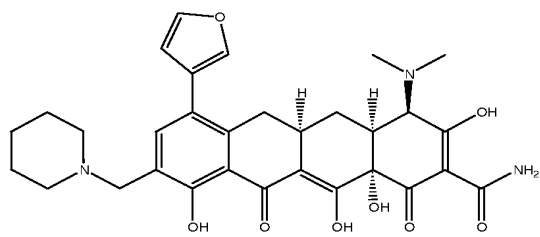


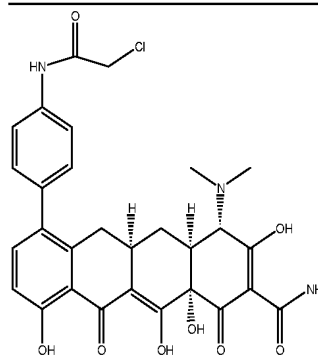
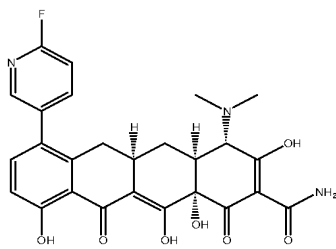
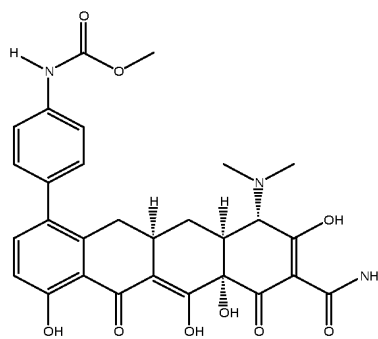
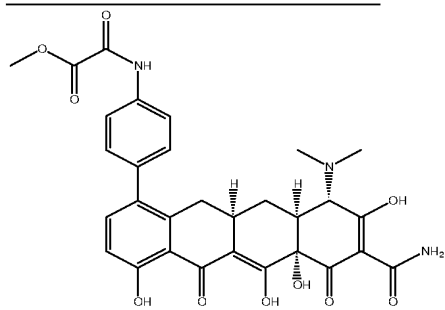
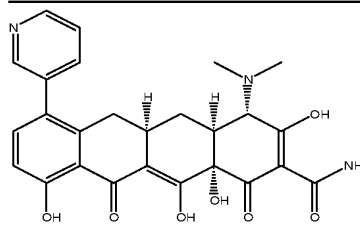
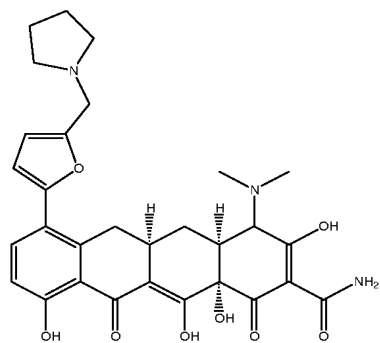
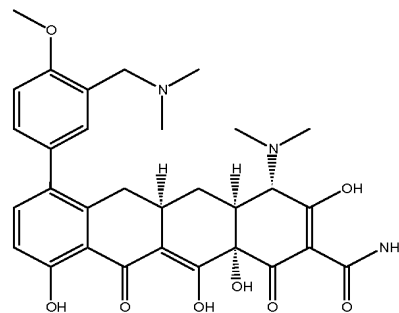
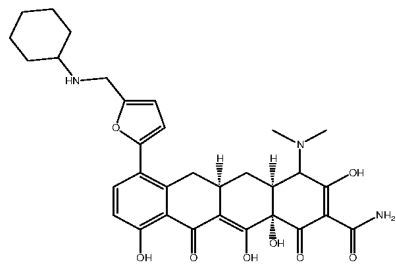
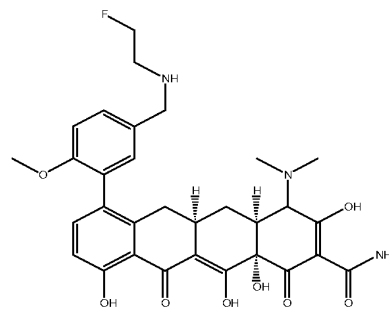
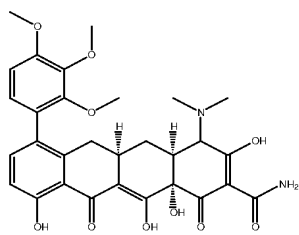


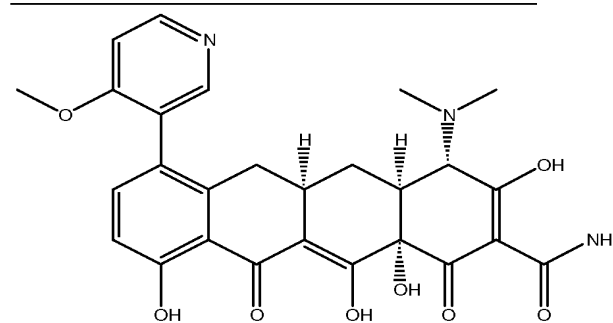
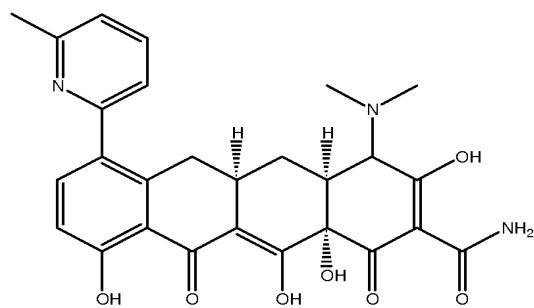
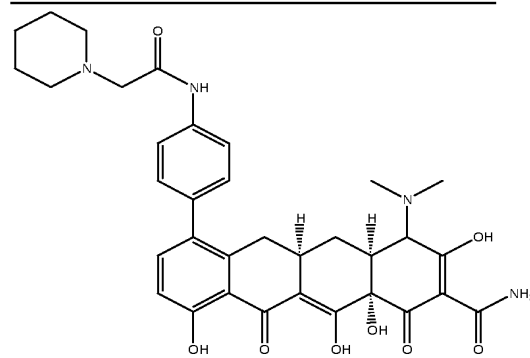
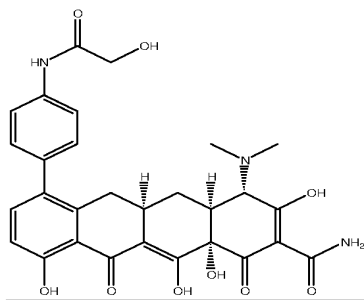
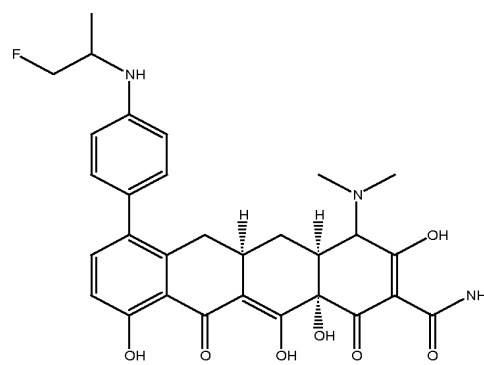
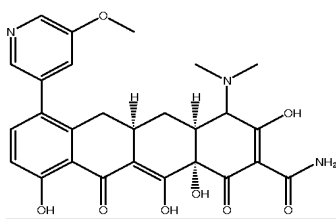
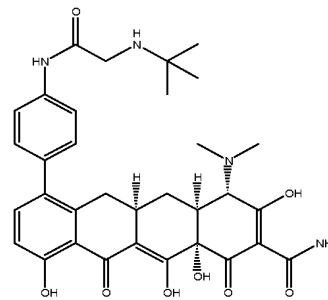
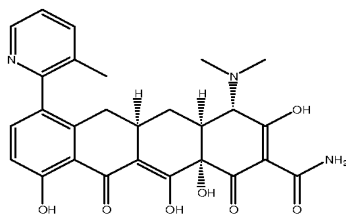
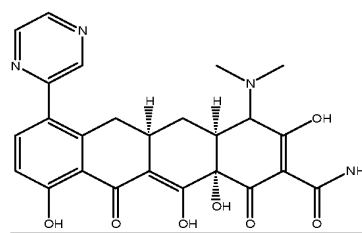
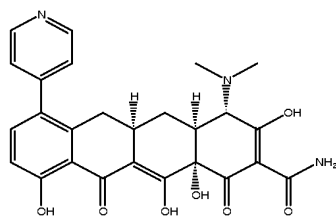


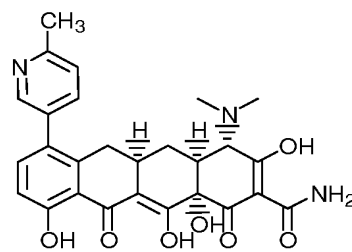
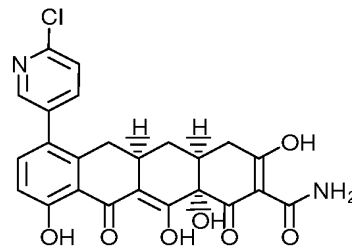
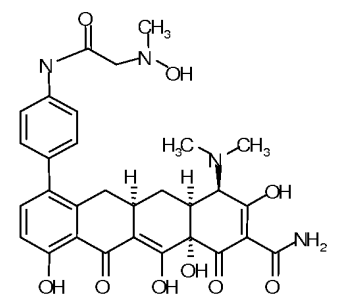
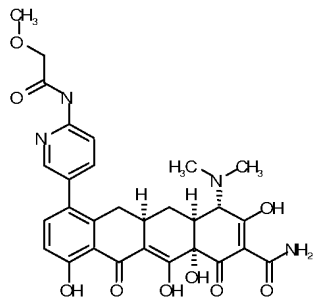
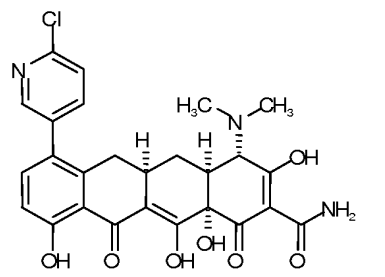
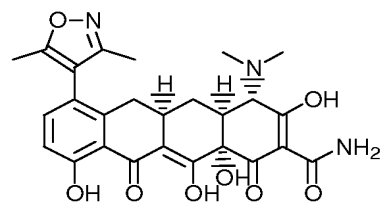
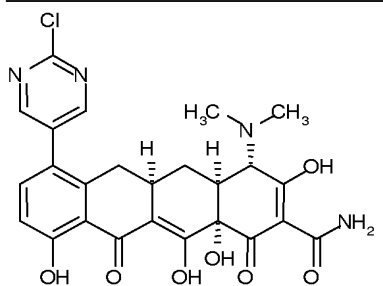
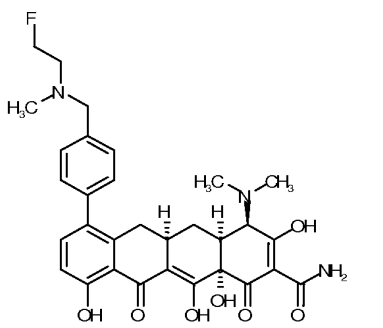
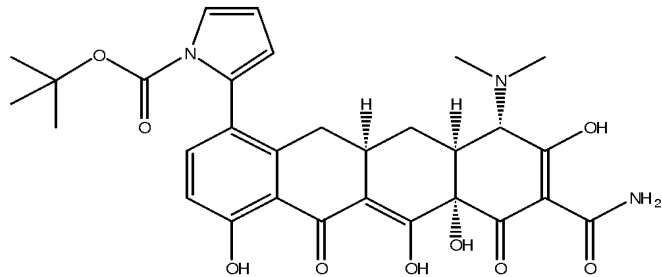
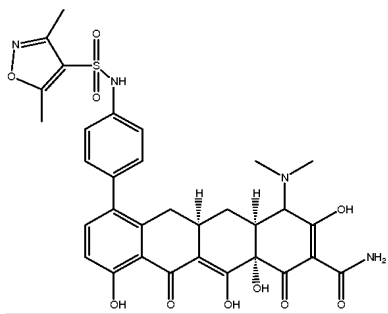


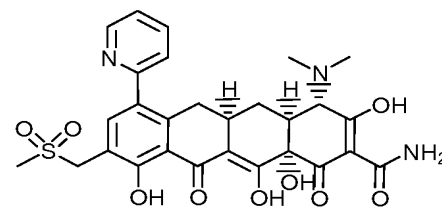
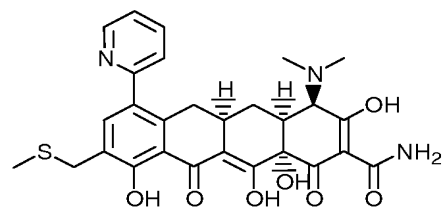
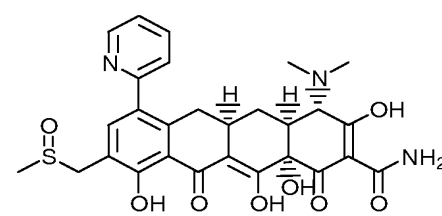
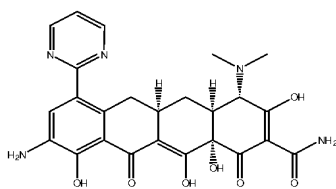
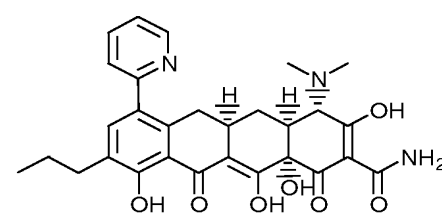
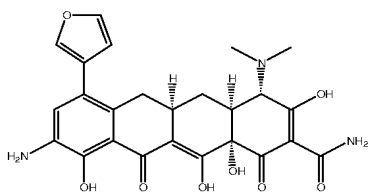
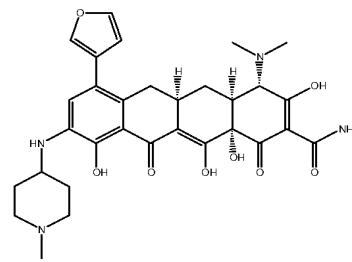
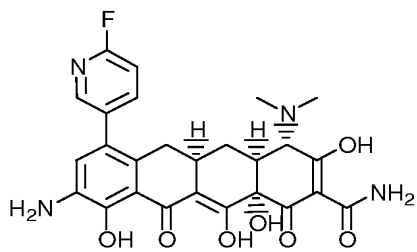
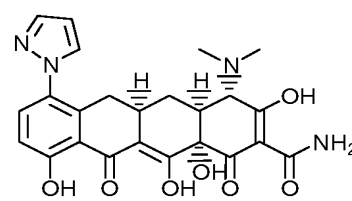
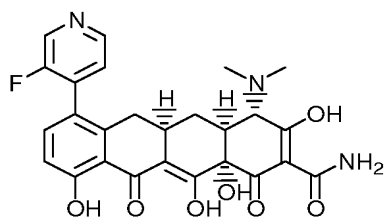


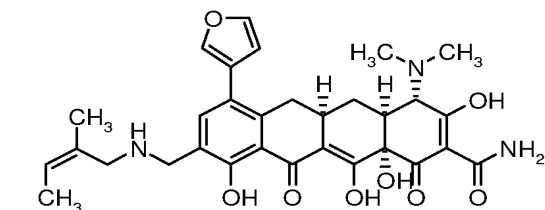
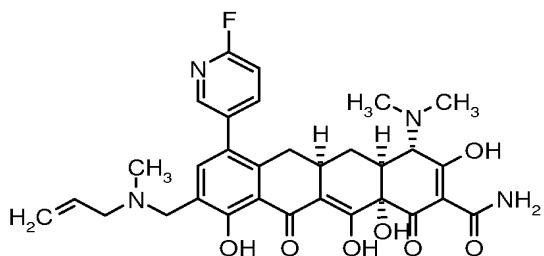
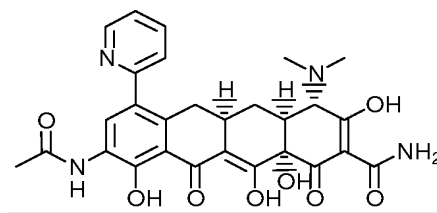
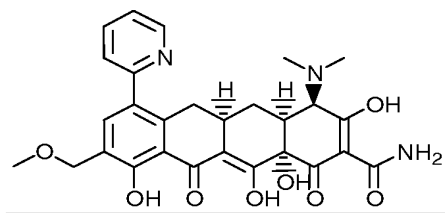
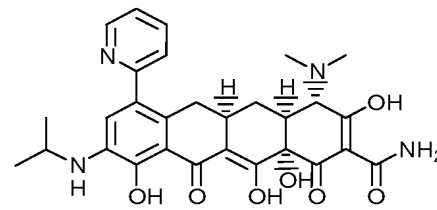
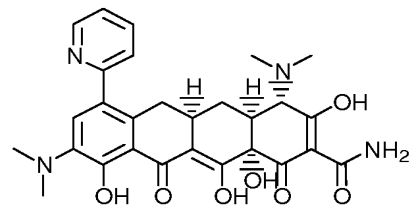
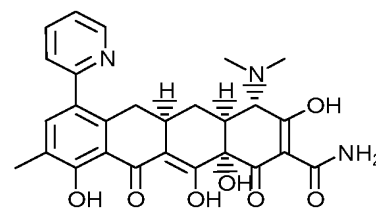
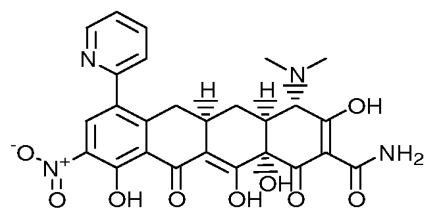


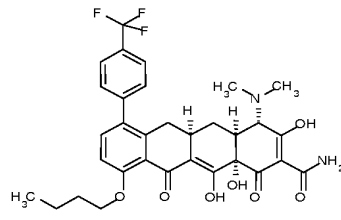
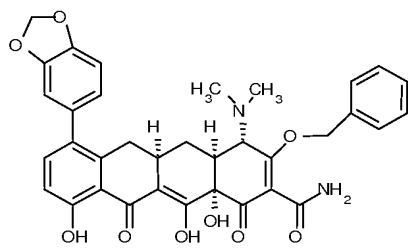
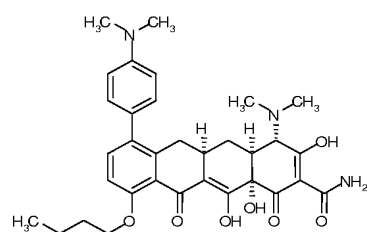
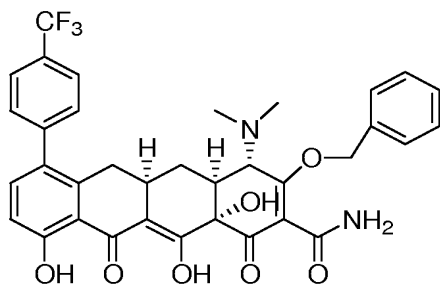
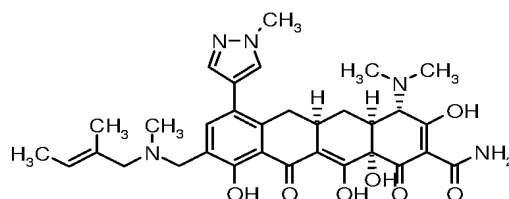
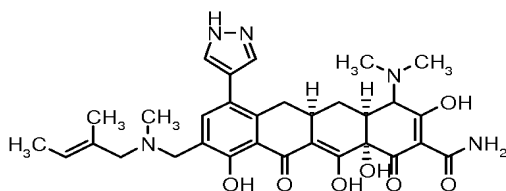
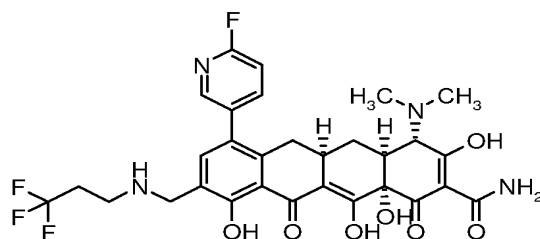
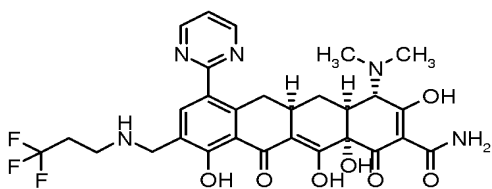
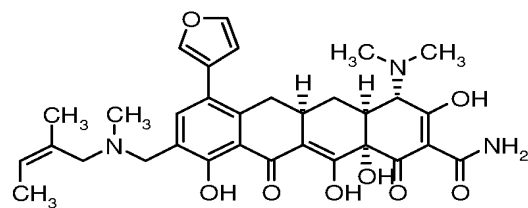
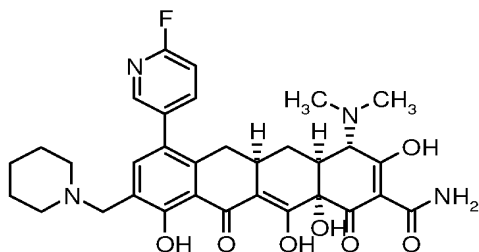


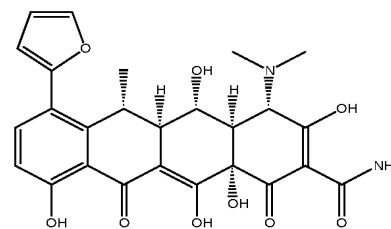
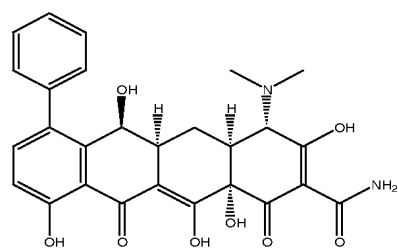
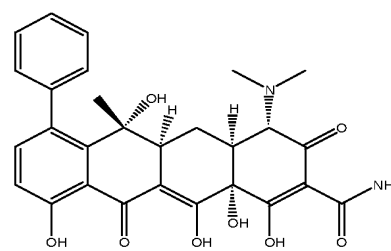
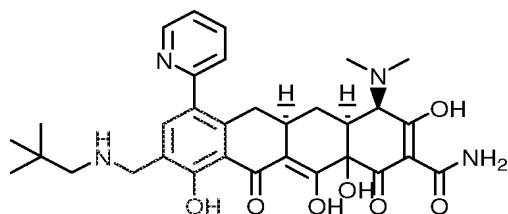
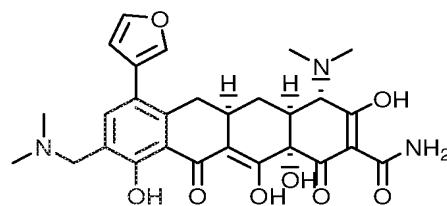
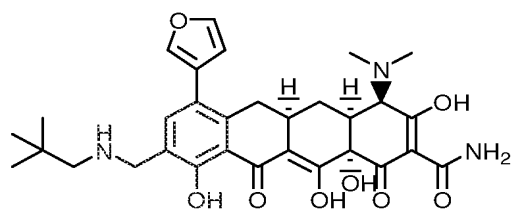
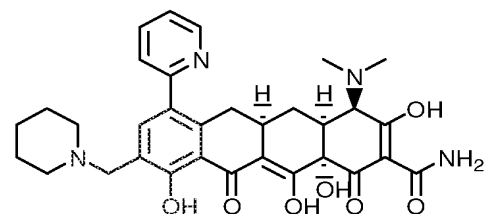
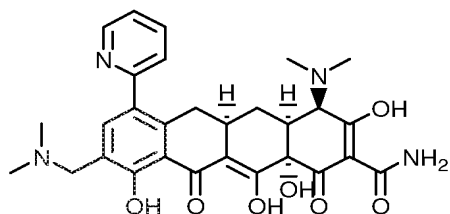
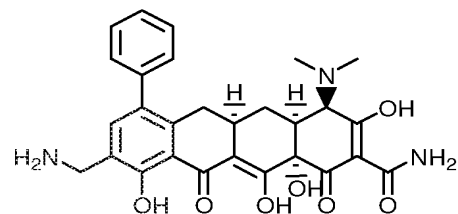
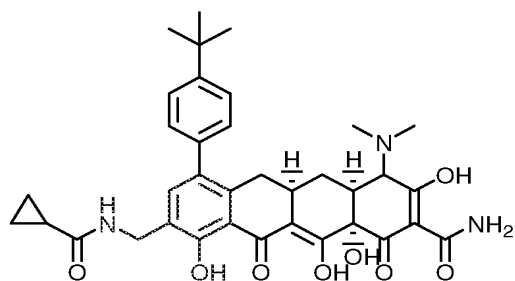


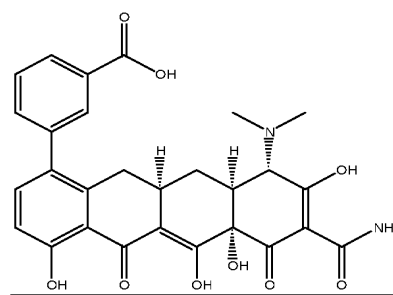
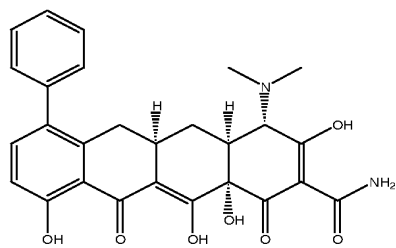
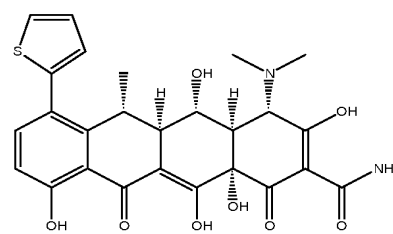
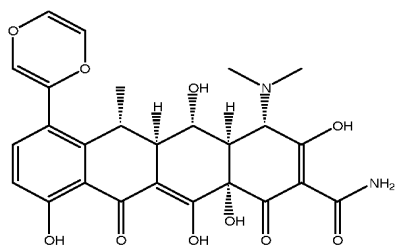
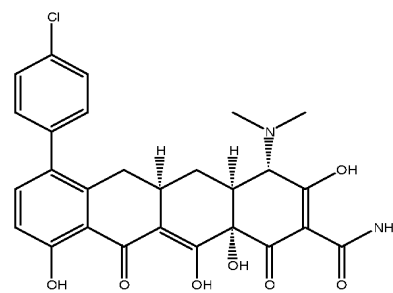
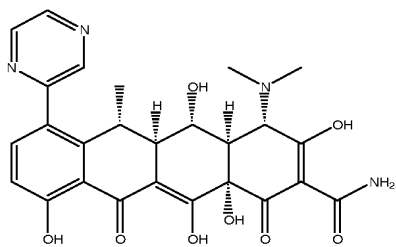
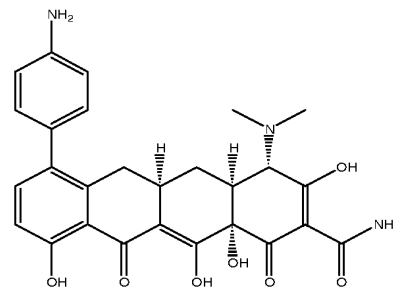
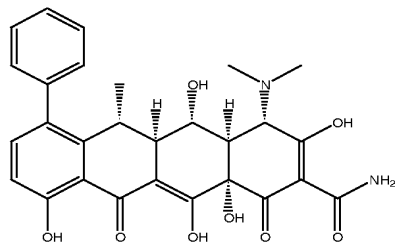
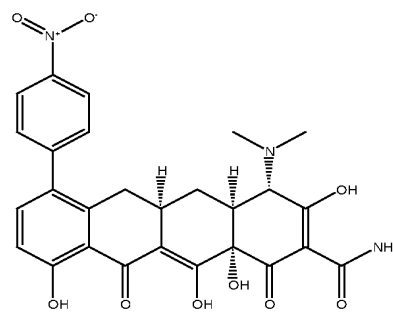
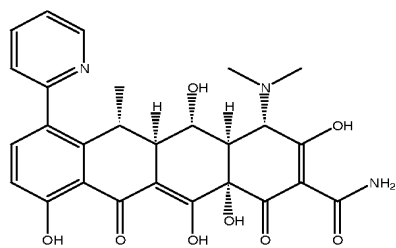


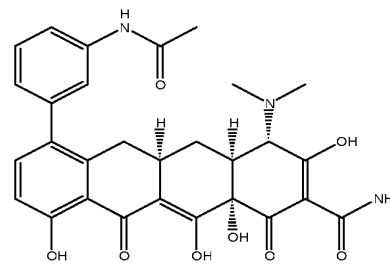
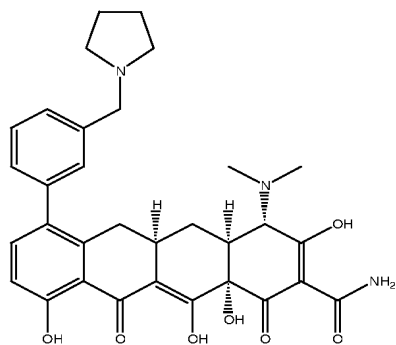
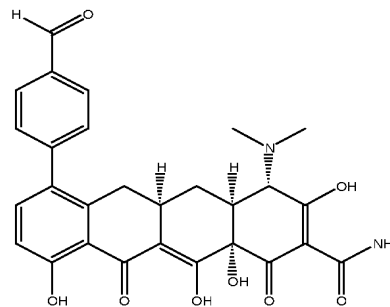
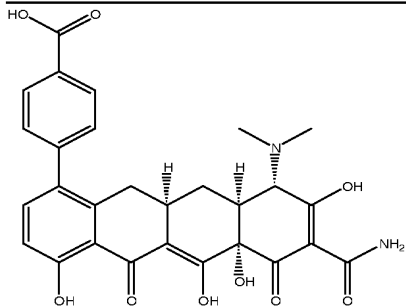
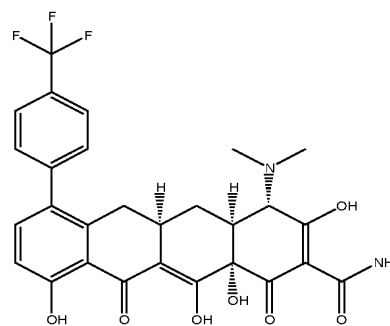
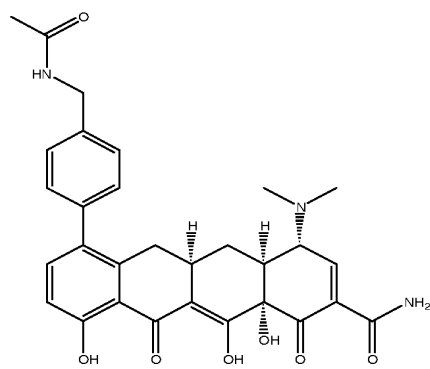
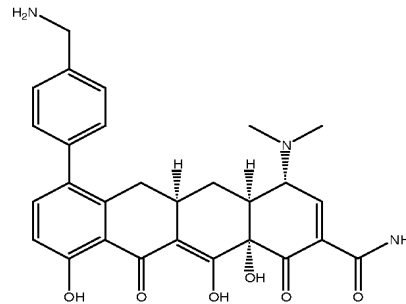
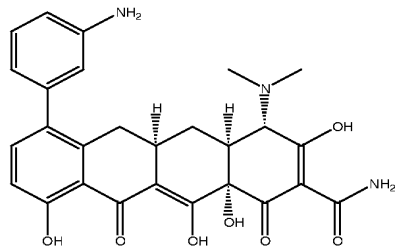
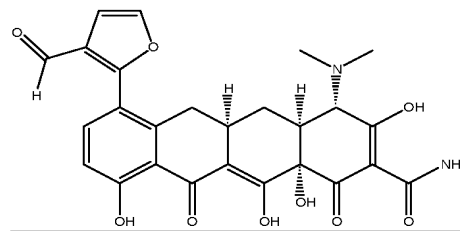
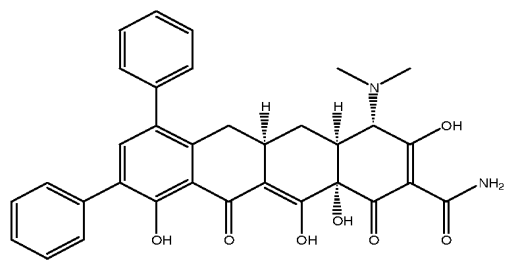


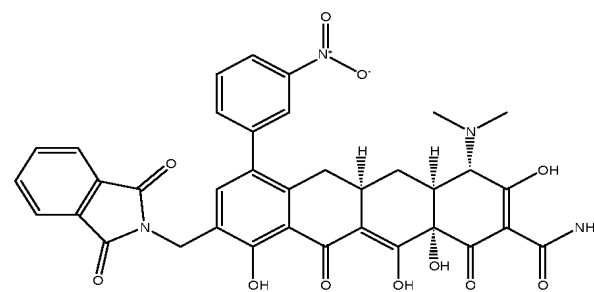
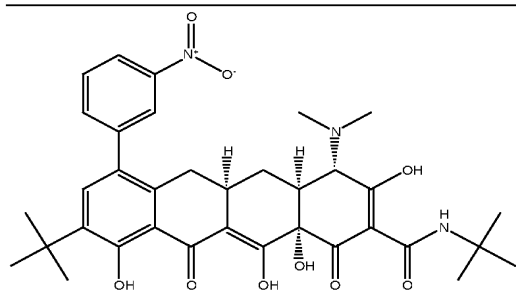
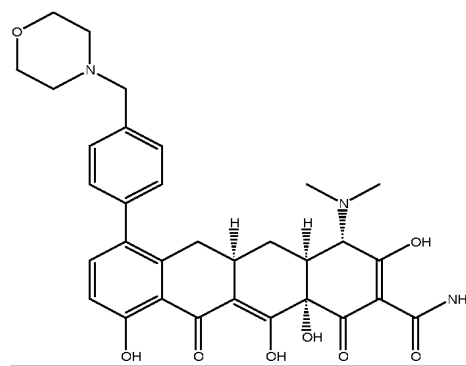
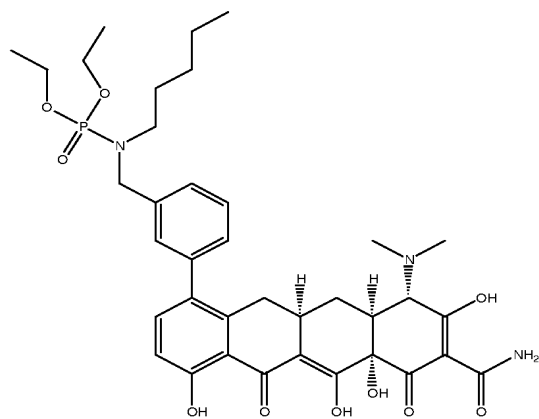
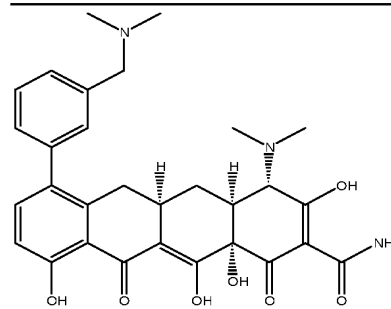
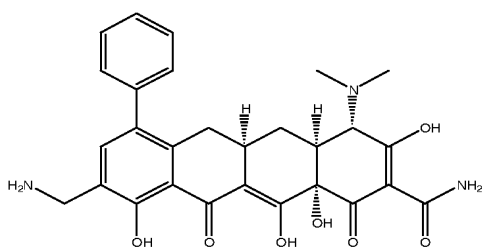
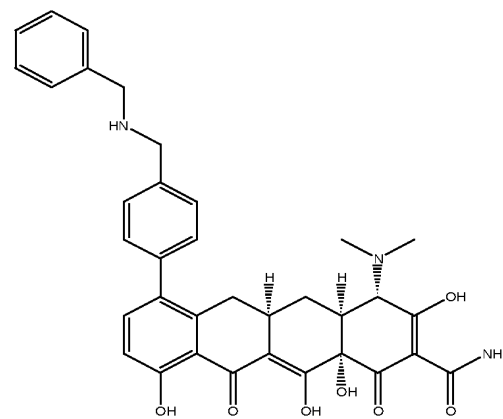
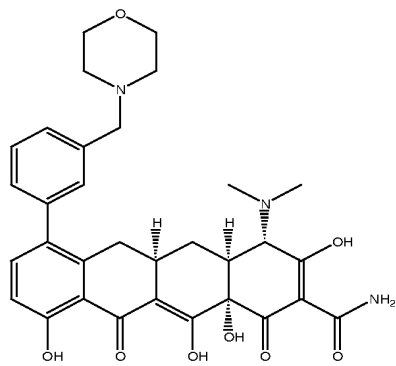


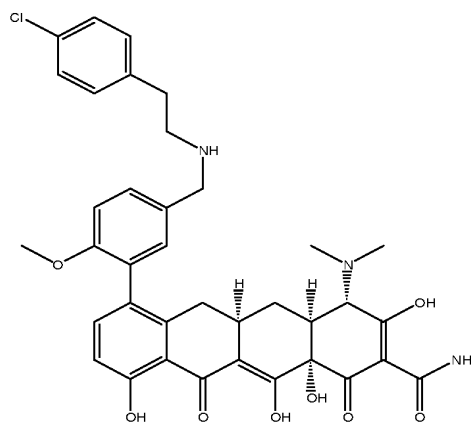
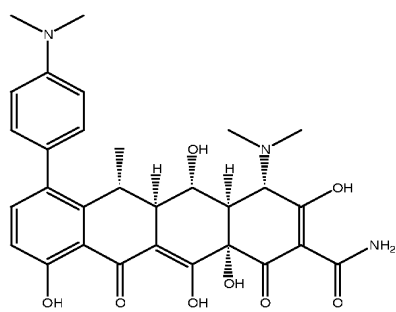
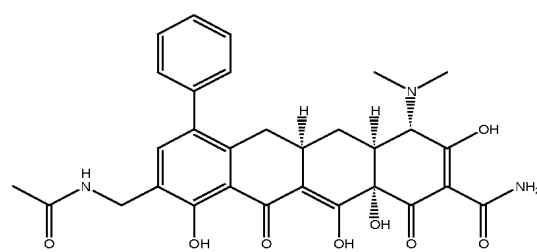
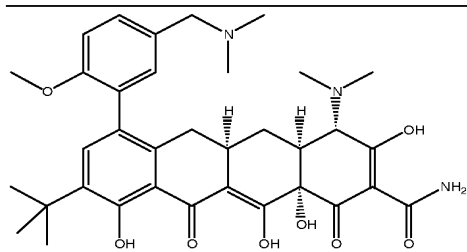
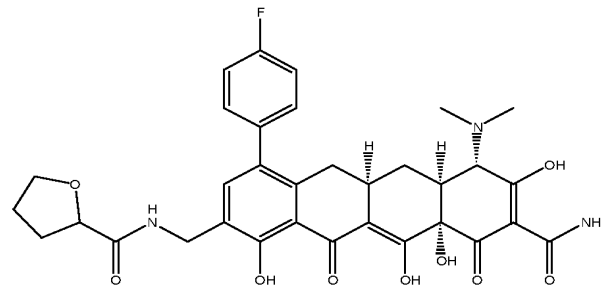
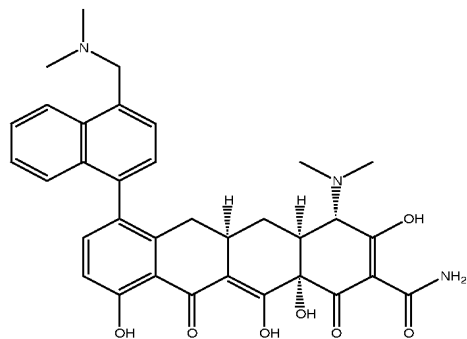
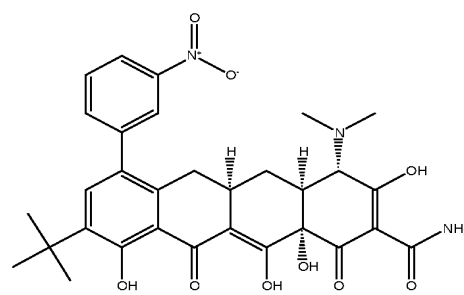
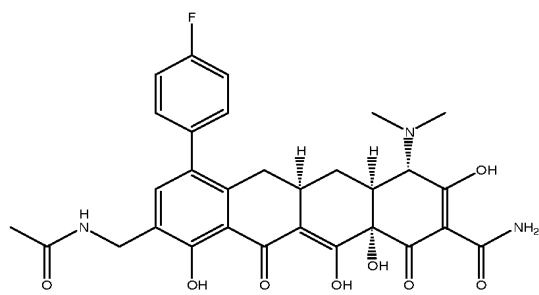


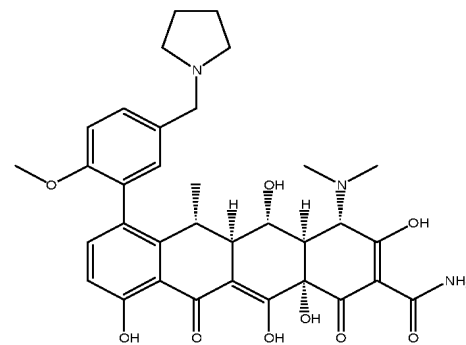
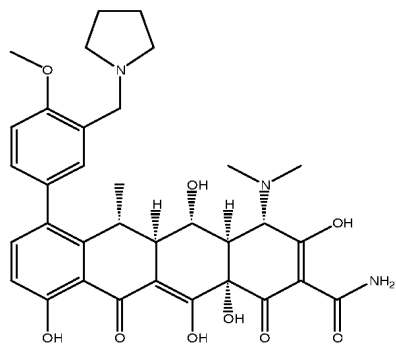
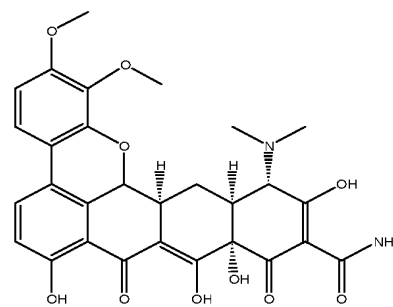
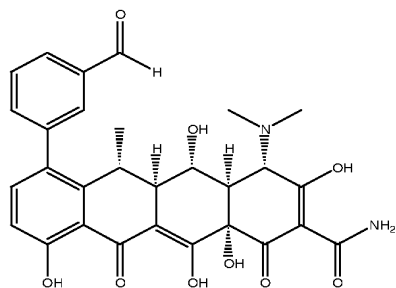
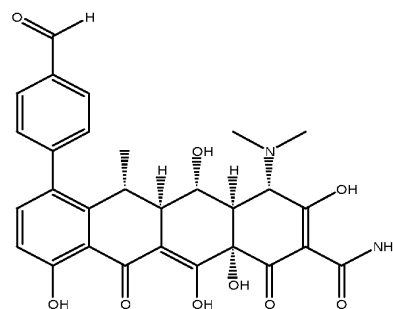
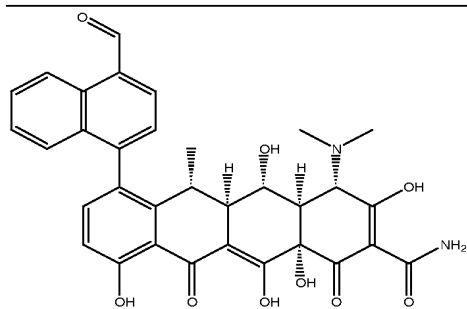
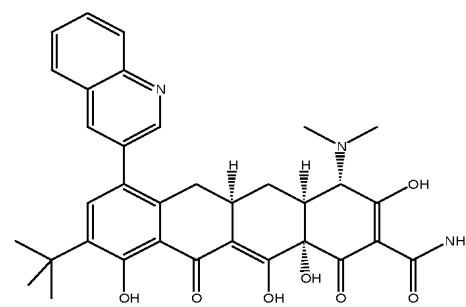
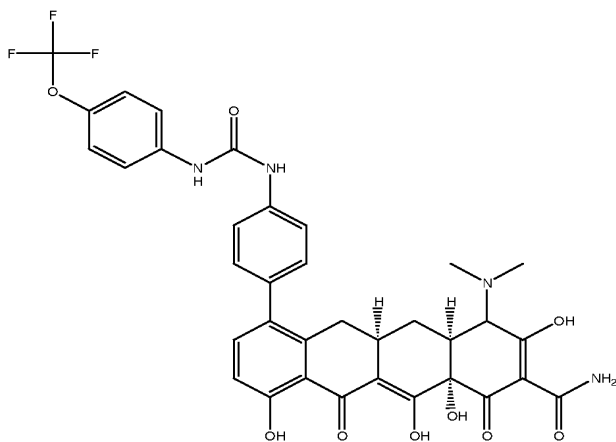


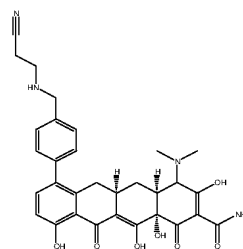
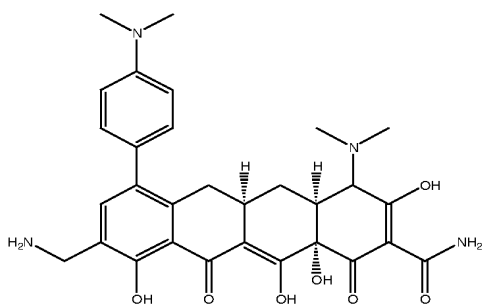
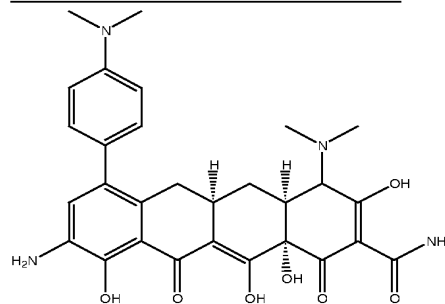
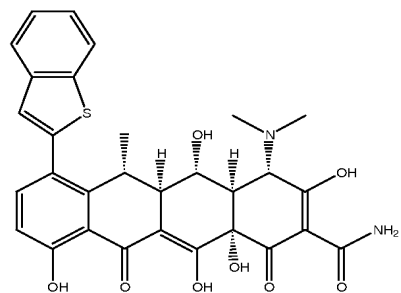
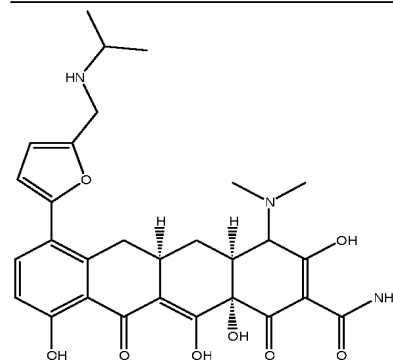
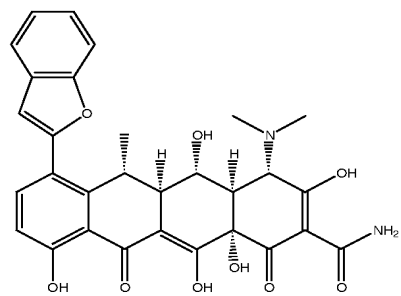
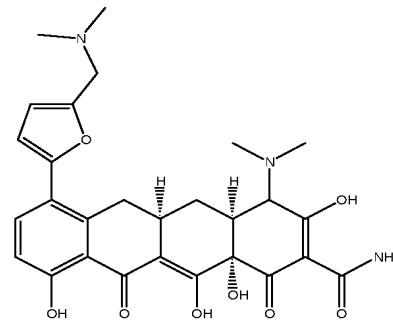
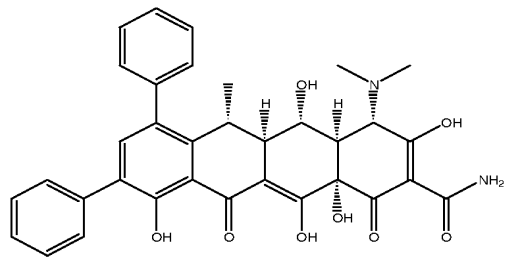
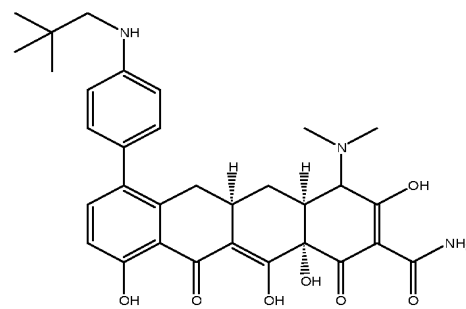
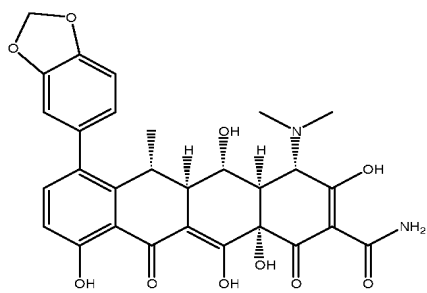


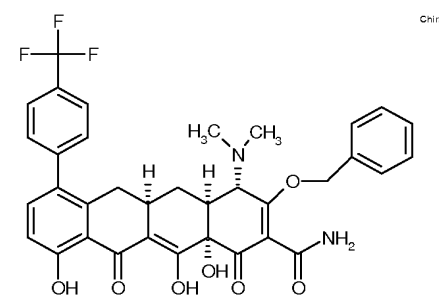
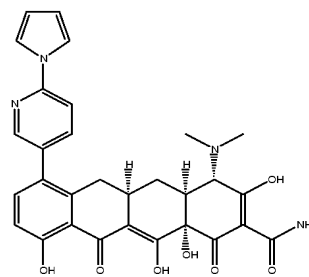
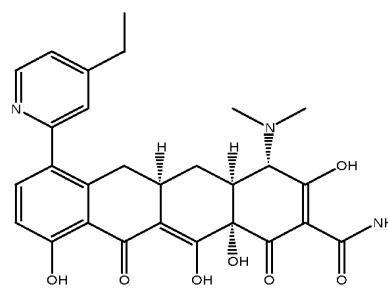
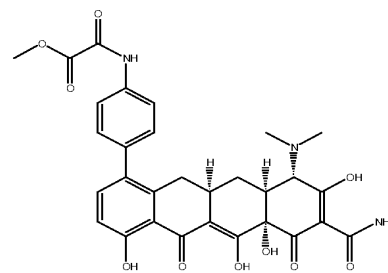
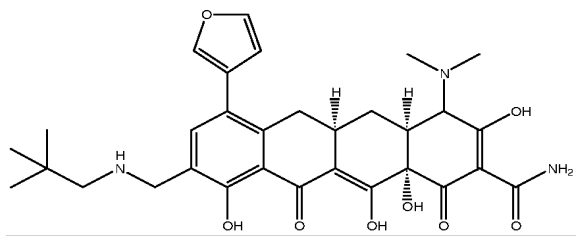
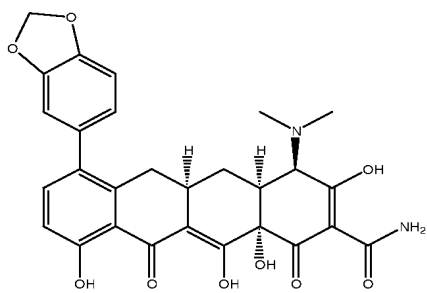
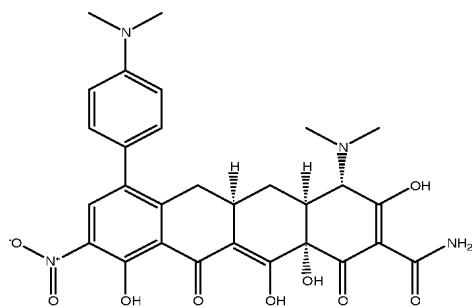
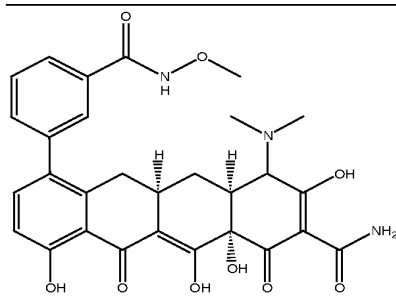
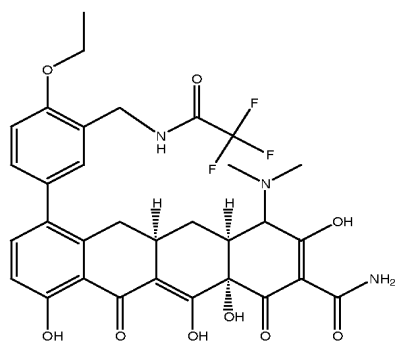




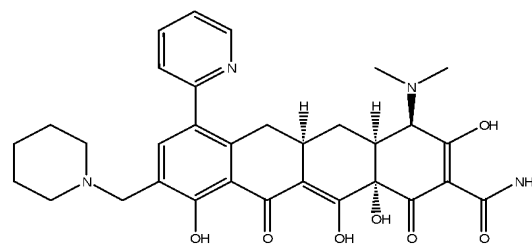


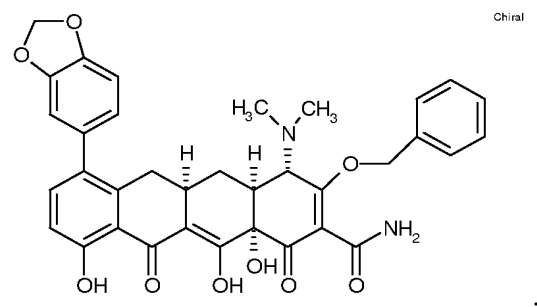
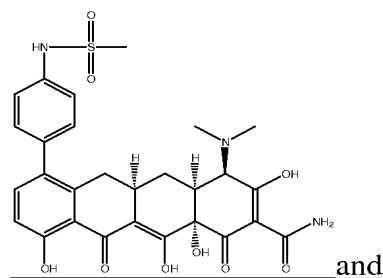
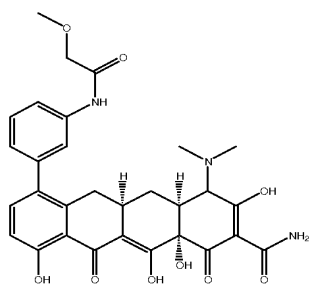
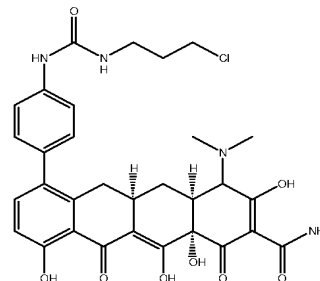
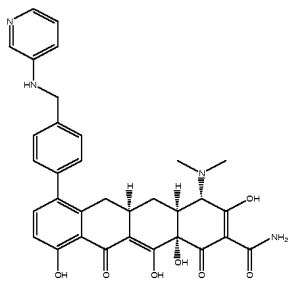
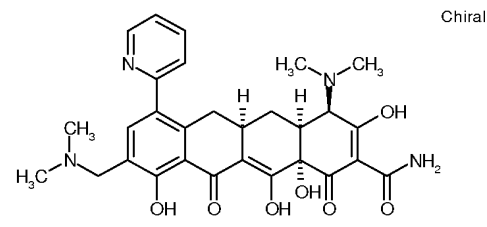
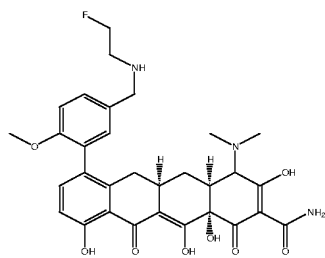






Chiral



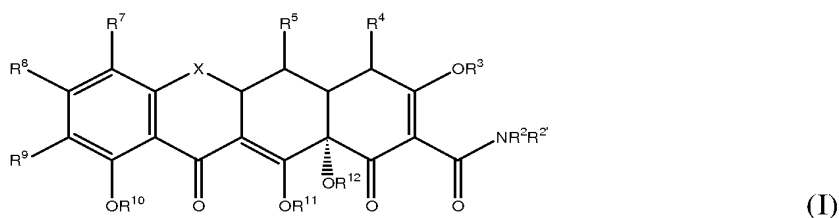


72. **(Original)** The method of claim 67 or 69, wherein said substituted tetracycline compound is non-antibacterial.

73. **(Original)** The method of claim 67 or 69, wherein said substituted tetracycline compound is has anti-microbial gram positive activity.

74. **(Original)** The method of claim 73, wherein said anti-microbial gram positive activity is greater than about 0.05 µg/ml.

75. **(Original)** The method of claim 74, wherein said anti-microbial gram positive activity is greater than about 5 µg/ml.
76. **(Original)** The method of claim 75, wherein said substituted tetracycline compound has a cytotoxicity of 25 µg/ml or greater.
77. **(Original)** The method of claim 67 or 69, wherein said substituted tetracycline compound has a MIC of 150 nM or less.
78. **(Original)** The method of claim 77, wherein said substituted tetracycline compound has a MIC of 50 nM or less.
79. **(Original)** The method of claim 78, wherein said substituted tetracycline compound has a MIC of 10 nM or less.
80. **(Original)** The method of claim 79, wherein said substituted tetracycline compound has an MIC of 5 nM or less.
81. **(Previously Presented)** A pharmaceutical composition comprising an effective amount of a substituted tetracycline compound to treat malaria in a mammal and a pharmaceutically acceptable carrier, wherein said tetracycline compound is of formula I:



wherein:

X is CR^{6'}R⁶;

R², R^{2'}, R^{4'}, and R^{4''} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ is NR^{4'}R^{4''}, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R³, R¹¹ and R¹² are each hydrogen, or a pro-drug moiety;

R¹⁰ is hydrogen, or a prodrug moiety;

R^5 is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and R^6' are independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is aryl;

R^9 is hydrogen;

R^8 is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and pharmaceutically acceptable salts thereof.

82. **(Previously Presented)** The pharmaceutical composition of claim 81, wherein said substituted tetracycline compound is selected from the group consisting of:

83. **(Cancelled)**

84. **(Original)** The pharmaceutical composition of claim 81, further comprising a secondary agent.

85. **(Original)** The pharmaceutical composition of claim 84, wherein the secondary agent is selected from the group consisting of proguanil, chlorproguanil, trimethoprim, chloroquine, mefloquine, lumefantrine, atovaquone, pyrimethamine-sulfadoxine, pyrimethamine-dapsone, halofantrine, quinine, quinidine, amodiaquine, amopyroquine, sulphonamides, artemisinin, arteflene, artemether, artesunate, primaquine, 1,16-hexadecamethylenebis(N-methylpyrrolidinium)dibromide and pyronaridine.

86. **(Cancelled)**

87. **(Previously Presented)** The method of claim 1, wherein the substituted tetracycline compound is

